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16. ABSTRACT

Section 304(A) of the Clean Water Act [33 U.S.C. 1314(A)], requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for Mercury. It presents concentration criteria for the protection of freshwater and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A Section 304(A) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no regulatory effect.

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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CRITERIA DOCUMENT

MERCURY

CRITERIA

Aquatic Life

For total recoverable mercury the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.00057 μg/l as a 24-hour average and the concentration should not exceed 0.0017 μg/l at any time.

For total recoverable mercury the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.025 μg/l as a 24-hour average and the concentration should not exceed 3.7 μg/l at any time.

Human Health

For the protection of human health from the toxic properties of mercury ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 144 ng/l.

For the protection of human health from the toxic properties of mercury ingested through contaminated aquatic organisms alone, the ambient water criterion is determined to be 146 ng/l.

Note: Criteria reflect ingestion of marine organisms as well as freshwater and estuarine fish and shellfish.

INTRODUCTION

Mercury, a silver-white metal which is a liquid at room temperature, can exist in three oxidation states: elemental, mercurous, and mercuric; it can be part of both inorganic and organic compounds.

Mercury is a silver-white metal, atomic weight 200.59. A liquid at room temperature, its melting point is -38.87°C and its boiling point ranges from 356 to 358°C. The metal is insoluble and is not attacked by water. At 20°C, the specific gravity is 13.546 (Stecher, 1968), and the vapor pressure is 0.0012 mm Hg (Stecher, 1968).

Mercury exists in a number of forms in the environment. The more commonly found mercuric salts (with their solubilities in water) are $HgCl_2$ (1g/13.5 ml water), $Hg(NO_3)^2$ (soluble in a "small amount" of water), and $Hg(CH_3COO)_2$ (1.0 g/2.5 ml water). Mercurous salts are much less soluble in water. $HgNO_3$ will solubilize only in 13 parts water containing 1 percent HNO_3. Hg_2Cl_2 is practically insoluble in water. Because of this, mercurous salts are much less toxic than the mercuric forms (Stecher, 1968).

The Department of the Interior carried out a nationwide reconnaissance of mercury in U.S. water in the summer and fall of 1970 (Jenne, 1972). Of the samples from the industrial wastewater category, 30 percent contained mercury at greater than 10 µg/l; nearly 0.5 percent of the samples in this group contained more than 1,000 µg/l. Only 4 percent of the surface water samples contained more than 1,000 µg/l. The higher mercury concentrations were generally found in small streams. About half of the 43 samples from the Mississippi River contained less than 0.1 µg/l. The mercury content of lakes and reservoirs was between 0.1 and 1.8 µg/l. With few exceptions, the mercury content of groundwater samples was below detection (0.1 µg/l).

In a survey by the Environmental Protection Agency (EPA) Division of Water Hygiene, 273 community, recreation, and Federal installation water supplies were examined. Of these, 261 or 95.5 percent, showed either no detectable mercury or less than 1.0 μg/l in the raw and finished water. Eleven of the supplies had mercury concentrations of 1.0 to 4.8 μg/l and one supply exceeded 5.0 μg/l. When this one supply was extensively reexamined, the mercury concentration was found to be less than 0.8 μg/l (Hammerstrom, et al. 1972).

Seawater contains 0.03 to 2.0 μg/l, depending on the sampled area, the depth, and the analyst. In a study of Pacific waters, mercury concentrations were found to increase from surface values of about 0.10 μg/l to 0.15, to 0.27 μg/l at greater depths. In an area seriously affected by pollution (Minamata Bay, Japan), values ranged from 1.6 to 3.6 μg/l. The National Research Council (1977) has shown typical oceanic values for mercury to be 0.01 to 0.03 μg/l. Oceanic mercury is generally present as an anionic complex ($HgCO^-$), which does not have as pronounced a tendency to bind to particulate substances and then settle out as do mercury compounds found in freshwater (Wallace, et al. 1971).

A major use of mercury has been as a cathode in the electrolytic preparation of chlorine and caustic soda; this accounted for 33 percent of total demand in the United States in 1968. Electrical apparatus (lamps, arc rectifiers, and mercury battery cells) accounted for 27 percent, industrial and control instruments (switches, thermometers, and barometers), and general laboratory applications accounted for 14 percent of demand. Use of mercury in antifouling and mildew proofing paints (12 percent) and mercury formulations used to control fungal diseases of seeds, bulbs, plants, and vegtetation (5 percent) were other major utilizations, however, mercury is no longer registered by the EPA for use in antifouling paints or for the control of fungal diseases of bulbs. The remainder (9 percent) was for dental amalgams, catalysts, pulp and paper manufacture, pharmaceuticals, and metallurgy and mining.

Several forms of mercury, ranging from elemental to dissolved inorganic and organic species, are expected to occur in the environment. The finding that certain microorganisms have the ability to convert inorganic and organic forms of mercury to the highly toxic methyl or dimethyl mercury has made any form of mercury highly hazardous to the environment (Jensen and Jernelov, 1969). In water, under naturally occurring conditions of pH and temperature, inorganic mercury can be coverted readily to methyl mercury (Bisogni and Lawrence, 1973).

Mercury is able to form a series of organometallic compounds with alkyl, phenyl, and methoxyethyl radicals. Short-chained alkyl mercurials are toxicologically important because the carbon-mercury bond can be broken in vivo, with the subsequent disappearance of the organic radical.

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Aquatic Life Toxicology*

INTRODUCTION

Mercury has long been recognized as one of the more toxic metals but only recently was it identified as a serious pollutant in the aquatic environment. Elemental mercury, which is a heavy liquid at room temperature, was considered relatively inert. It was thought that it would quickly settle to the bottom of a body of water and remain there in an innocuous state. However, elemental mercury can be oxidized in sediment to divalent mercury (Wood, 1974). Furthermore, both aerobic and anaerobic bacteria have been found capable of methylating divalent mercury in sediments (The National Research Council, 1978) and estuarine areas (Jernelov, 1971). This methylated form is more water soluble and more biologically active than elemental and inorganic divalent mercury (Fromm, 1977; Armstrong and Scott 1979; Jernelov, et al. 1975). Largely because of bacterial methylation, mercury is much more of a serious threat to the aquatic environment than was suspected. Mercury is one of the few pollutants that, at about the same concentrations in water, adversely affects aquatic life through direct toxicity and affects uses of aquatic life through bioaccumulation. Bioaccumulation has received more attention because of potential adverse effects to humans. Methylmercury is more toxic than inorganic mercury to mammals as well as aquatic life, and mercury has no known physiological function.

The toxicological data base and environmental chemistry of mercury suggest that divalent inorganic mercury (inorganic mercury) and monomethyl mercury (methylmercury) are the forms that are most directly hazardous to aquatic systems. Even in situations in which no organic mercury was known to have been discharged, methylmercury was the dominant form in tissue residues (Jernelov and Lann, 1971).The methylated form is of great concern because it comprises most of the mercury residue in tissues of aquatic organisms (Hattula, et al. 1978; Cappon and Smith, 1979) and tissue residues are a potential hazard to consumers of aquatic life. Defining the toxicity of mercury residues to humans, and probably other consumers of aquatic life, is complicated by the effect of selenium on the toxicity of mercury (Strom, et al. 1979; Friedman, et al. 1979; Cappon and Smith, 1979; Speyer, 1980; Ganther, et al. 1972a, 1972b,; Luten, et al. 1980, and Rudd, et al. 1980), especially when it is known that aquatic organisms from different sources have substantially different selenium to mercury ratios. The FDA action level of 1.0 mg/kg based on saltwater fish may be too high for freshwater fish which have significantly different selenium to mercury ratios.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are calculations for deriving various measures of toxicity as described in the Guidelines.

Once methylation takes place, uptake by aquatic life is extremely rapid, and demethylation is a very slow process (McKim et al. 1976). Depuration by excretion through the kidney reportedly requires demethylation (Burrows and Krenkel, 1973). Apparently the slow rate of demethylation is responsible for mercury's biological half-life of approximately 2 to 3 years (Lockhart, et al. 1972; McKim, et al. 1976). In freshwater fishes, initial elimination of mercury just after the end of exposure is relatively rapid, due to sluffing of the slime coat (Burrows and Krenkel, 1973) and elimination of non-methylated mercury. Once methylmercury becomes securely bound to sulfhydryl groups in muscle proteins, subsequent loss proceeds at a much reduced rate. In fact, long term reduction of the concentration of mercury in fish tissue is largely due to dilution by tissue addition resulting from growth (Lockhart, et al. 1972; McKim, et al. 1976).

Methylation of inorganic mercury has been demonstrated in the environment, in the slime coat of fishes, and in the intestines of fish (Jernelov, 1968), but has not been demonstrated to occur once the mercury is absorbed into tissues of fish (Pennarcchioni, et al. 1976; Huckabee, et al. 1978). High mercury concentrations in slimy freshwater fishes such as burbot, eels, and northern pike, and in the skin of acutely-exposed fishes are believed due to the methylating activity of bacteria prevalent in the mucous coat (Jernelov, 1968). Acutely toxic concentrations of mercury have been reported to stimulate mucous secretion (McKone, et al. 1971; Baker, 1973), resulting in the belief by some that the skin and its mucous coat are proportionately greater mercury sinks than other fish tissues (Burrows, et al. 1974). However, these are the layers of the fish that are first encountered as mercury moves from the environment into a fish, and in acute exposures the mercury does not have time to be transported to the final sink - the proteins whose greatest mass are in the axial muscle (McKim, et al. 1976).

Numerous data are available concerning the effect of phenylmercuric acetate (PMA) on aquatic organisms, because of its use as a fungicide and its use to treat fish diseases. Many tests have been conducted on different PMA formulations which contain various percentages of active ingredient. The percentages of active ingredient given by the authors were used to convert to concentrations of mercury. When the percentage of active ingredient was not given, 80 percent PMA was assumed (Allison, 1957).

Of the analytical measurements currently available, water quality criteria for mercury are probably best stated in terms of total recoverable mercury, because of the variety of forms of mercury than can exist in bodies of water and the various chemical and toxicological properties of these forms. The forms of mercury that are commonly found in bodies of water and are not measured by the total recoverable procedure, such as the mercury that is a part of minerals, clays and sand, probably are forms that are less toxic to aquatic life and probably will not be readily converted to the more toxic forms under natural conditions. On the other hand, forms of mercury that are commonly found in bodies of water and are measured by the total recoverable procedure, such as the free ion, the hydroxide, carbonate, and sulfate salts, and the organic compounds, probably are forms that are more toxic to aquatic life or can be converted to the more toxic forms under natural conditions. Because the criteria for mercury are derived on the basis of tests conducted on soluble inorganic salts of divalent inorganic mercury and monomethylmercuric chloride, the total and total recoverable concentrations in the test should be about the same. Except as noted, all concentrations reported herein are expected to be essentially equivalent to total recoverable mercury. All concentrations are expressed as mercury, not as the compound.

EFFECTS

Acute Toxicity

Table 1 contains the primary acute toxicity data for three classes of mercury compounds: inorganic mercuric salts, methylmercuric compounds, and other mercury compounds, chiefly organic. The latter information exists principally because many of these compounds have been used for disease treatment and parasite control in fish cultural practices, though their source for environmental concern is from industrial and agricultural uses for fungus control. A striking feature of the freshwater acute toxicity values is that the difference in sensitivity between different types of organisms to a particular mercury compound is far greater than the difference in sensitivity of a particular species to various mercury compounds. For inorganic mercury, the reported 96-hour LC_{50} values range from 0.02 µg/l for male crayfish to 2,000 µg/l for larvae of a caddisfly, with a continual gradation in sensitivity among species with intermediate sensitivities (Table 3). Data are insufficient to make such comparisons for other two classes of mercury compounds. Rainbow trout are the most acutely sensitive of the tested fish species to all three kinds of mercury compounds and methylmercuric chloride is about ten times more acutely toxic to rainbow trout than is mercuric chloride.

MacLeod and Pessah (1973) studied the effect of temperature on the acute toxicity of mercuric chloride to rainbow trout. At 5, 10, and 15°C, the LC_{50} values were 400, 280, and 220 µg/l, respectively. Clemens and Sneed (1958) found similar temperature effects with mercury exposures at 10, 16.5, and 24°C (Table 6). Their acute values for phenylmercuric acetate were 1,960, 1,360, and 233 µg/l, respectively, with juvenile channel catfish.

A freshwater Final Acute Value of 0.0017 µg/l was obtained for inorganic mercury using the species mean acute values in Table 3 and the calculation procedures described in the Guidelines. This value should be useful because it is based on data for eleven species, even though acute data are not available for any non-salmonid fish.

Acute values for mercuric chloride are available for 26 species of saltwater animals from 5 phyla (Table 1). Species mean acute values in Table 3 show that winter flounder is the most resistant species tested (LC_{50} = 1,680 µg/l) and the mysid shrimp the most sensitive (LC_{50} = 3.5 µg/l). Fishes were generally more resistant to mercuric chloride than the crustaceans and molluscs. The saltwater Final Acute Value for inorganic mercury, derived from the species mean acute values in Table 3 using the calculation procedures described in the Guidelines is 3.7 µg/l. Only one test with methylmercuric chloride has been reported with an acute value of 150 µg/l for the amphipod, Gammarus duebeni.

Chronic Toxicity

Chronic toxicity tests with Daphnia magna have been conducted on three different kinds of mercury compounds and the chronic values were all between 1.0 and 2.47 µg/l (Table 2). In addition, a chronic test with brook trout yielded a value of 0.52 µg/l for methylmercuric chloride. Of the three available acute-chronic ratios, values of 2.7 and 3.9 were obtained for mercuric chloride with Daphnia magna, whereas 140 was found for methylmercuric chloride with brook trout.

A chronic value of 1.2 µg/l has been determined (Table 2) from a flow-through life-cycle exposure of the mysid shrimp to mercuric chloride (U.S. EPA, 1980). Groups of 30 juvenile shrimp were reared in each of 5 concentrations for 36 days as 21°C and 30 g/kg salinity. Responses examined included time of appearance of first brood, time of first spawn, and productivity (total number of young/number of available female spawning days and total number of spawns/number of available female spawning days). No spawning occurred at 2.51 µg/l. Time to spawn and productivity were significantly ($P<0.05$) different at 1.66 µg/l compared to controls. The highest concentration at which no adverse effect on reproductive processes was detected was 0.82 µg/l. The chronic limits are 0.82 and 1.66 µg/l and the chronic value is 1.2 µg/l. The 96-hour LC_{50} for this species in the same study was 3.5 µg/l giving an acute-chronic ratio of 2.0.

The species mean acute-chronic ratio for Daphnia magna is 3.2, whereas that for mysid shrimp is 2.9, and these are both sensitive species in fresh and saltwater, respectively. All of the reported acutely sensitive species in both waters are invertebrate species. Thus the absence of an acute-chronic ratio for a fish species should not be too serious, and 3.0 can be used as the Final Acute-Chronic Ratio (Table 3). Division of the Final Acute Values by 3 results in freshwater and saltwater Final Chronic Values of 0.00057 and 1.2 µg/l, respectively.

Plant Values

Data concerning the toxicity of mercury compounds to freshwater aquatic plants are contained in Table 4 with some additional results in Table 6. Whereas plant values for inorganic mercury range from 80 to 2,600 µg/l effects due to methylmercury occur at concentrations as low as 4.8 µg/l. Another form of methylated mercury cause effects at concentrations less than 0.3 µg/l (Table 6). Although freshwater plants are relatively insensitive to inorganic mercury and sensitive to some of the methylated forms, they do not appear to be more sensitive to the respective forms of mercury than are freshwater animals.

Data describing the toxicity of mercuric chloride to saltwater plants are from two studies with seven species of algae. In both cases, growth was the response parameter investigated. The EC_{50} concentrations (Table 4) indicate reduction in growth at concentrations ranging from 10 to 160 µg/l. No data were found concerning the toxicity of organic mercury compounds to saltwater plant life.

Residues

Bioconcentration is a function of uptake rate relative to depuration rate. The bioconcentration factor for mercury is high because uptake is fast and elimination is very slow. Temperature accelerates uptake of mercury by increasing the metabolic rate and the respiratory volume. Because the gills are the primary surface for absorption of waterborne substances by freshwater aquatic organisms, uptake increases as respiratory volume increases. Increased metabolic rate also increases energy demand and thus increases food consumption. With greater rates of food comsumption, exposure to mercury through the food chain is accelerated (Sharpe, et al. 1977). Studies have shown that uptake through both the gills and the digestive tract are significant for fish, and some data suggest that tissue residues are higher in organisms exposed via both routes than via either separately (Boudou, et al. 1979; Phillips and Butler, 1978).

Because metabolic rate is important in mercury uptake, dissolved oxygen concentration could also be expected to influence uptake by increasing respiratory volume. In a recent study, low dissolved oxygen concentration in an eutrophic lake forced fishes into warmer surface water to secure adequate oxygen. In the warmer surface water the stimulated metabolic rate apparently increased mercury uptake (Larson, 1976).

Temperature may significantly affect uptake during episodic exposures to mercury in which steady-state is not reached in the organism. Under such conditions tissue residues are directly related to temperature (Reinert, et al. 1974). In addition, a direct relationship seems to exist between temperature and tissue residues after steady-state has been reached (Cember and Curtis 1978; Boudou, et al. 1972). The latter is difficult to understand if steady-state occurs at saturation of available bonding sites, but empirically is does seem to be the case (Murray, 1978). Apparently not only are uptake and depuration accelerated by termperature but, because of the disparity in rates between the two processes, higher tissue residues accumulate at higher temperature.

The differences in bioconcentration between different species of fish are thought to result from a number of causes: concentration in the food (Phillips and Buhler, 1978); the quantity of food consumed; the temperature at which the fish is living; and the differences in the mucous coat of different species (Jernelov, 1968). However within a given environment, bioconcentration factors for both forage and game fish tend to be similar (Huckabee, et al. 1974).

Distribution of mercury within a fish can conceptually be considered as a flowing system in which the flow pattern moves from the absorbing surfaces (the gills, skin, and gastrointestinal tract), into the blood, then to the internal organs and eventually either to the kidney or bile for elimination or to the muscle for long-term storage. The later storage site can be considered to have a small leak whereby mercury, after demethylation, re-cycles back to the kidney for excretion (Burrows and Krenke, 1973). This leak appears to be responsive to internal mercury "pressure" because, as steady-state is approached, accumulation rate is slowed either by a reduced uptake rate or an increased discharge rate. Internal "pressure" may inhibit membrane transport rates or, for a lack of storage sites, shunt mercury to elimination.

At steady-state, when tissue residues are relatively stable in the various organs, muscle mass composes such an important portion of the total fish mass that mercury concentrations in the portion of the total fish mass that mercury concentrations in the whole fish are similar to those in edible portions alone (McKim, et al. 1976; Huckabee, et al. 1974). However, acute exposures result in disproportionately high levels of mercury in the skin of fishes. This is probably due at least in part to the large amount of mucous which is secreted during acute exposures. In addition, in acute exposures the mercury is not given sufficient time to move from the absorbing surfaces to the muscle depot, as would be the case in most naturally occurring situations. When the acutely exposed fish are moved to mercury-free water, the skin quickly loses mercury (Burrows, et al. 1974) probably because most of the mercury associated with the tissue is being sluffed off, metabolically eliminated, or moved to a more enduring destination in protein storage.

The available freshwater bioconcentration factors (BCF) are contained in Tables 5 and 6. Table 5 contains BCF values only from those studies in which the exposure concentrations were measured and the tissue residues reached steady-state. The BCF data presented in Table 6 do not meet these stringent conditions but are used to provide information on BCF values for plants and to illustrate the very important influence of temperature on uptake and bioconcentration factors.

With brook trout the BCF for muscle is about the same or higher than that for whole body (McKim, et al. 1976). The BCF for muscle of brook trout at 273 days is the geometric mean of three values, 17,000, 21,000, and 33,000 at water concentrations of 0.29, 0.09, and 0.03 µg/l respectively. Those derived at concentrations of 0.93 µg/l and above were omitted because the fish were adversely affected. The decrease in BCF as the concentration in water increases may be largely an artifact of the mathematical derivation of the BCF. If the protein binding sites are saturated at all three concentrations, as would be expected at steady-state (Cember and Curtis, 1978), then the concentration of mercury in the tissue would be same at all concentrations of mercury in water. In this situation the BCF would be inversely proportional to the concentration in water.

Olson, et al. (1975) obtained a BCF of 63,000 with fathead minnows at 25°C. The contrast between fathead minnows (Olson, et al. 1975) and brook trout (McKim, et al. 1976) is one of considerable interest and potential importance. The trout were fed pelleted feed, and so little opportunity existed for food chain input to the trout. In contrast, the fathead minnow is a browser and had the opportunity not only to feed on the introduced food but also on the Aufwuchs growing within the mercury-enriched environment of the exposure chamber. The higher bioconcentration factor of 63,000 for the fathead minnows may be more representative of field situations in which fish are exposed to mercury via both the water and food routes (Phillips and Buhler, 1978; Phillips and Gregory, 1979). Furthermore, the fathead minnows were exposed at a temperature that would provide uptake and tissue residue values representative of the higher range of temperatures for fish commonly consumed by people. On the other hand, if the concentration of mercury in fish tissue at steady-state is solely dependent on the number of available binding sites, then such things as temperature should not affect the BCF.

Boudou et al. 1979, also provide data demonstrating the importance of both routes of exposure on resulting BCF values (Table 6). In addition, they studied the influence of temperature on uptake when both respiratory and feeding rates are accelerated by increased metabolism. Reinert, et al. (1974) reported 84-day BCF values of 4,530, 6,620, and 8,049 in rainbow trout exposed to virtually equal concentrations of methylmercury at 5, 10 and 15°C, respectively, although residue concentrations were still increasing at the end of the test. Cember and Curtis, (1978) obtained similar effects when bluegills were exposed for 28.5 days. BCF values of 373, 921, and 2,400 were obtained at 9, 21, and 33°C, respectively. They suggested that a Q10 relationship exists between temperature and BCF.

The FDA action level for mercury in fish and shellfish is 1.0 mg/kg (Table 5). According to the Guidelines for freshwater organisms the only appropriate BCF available for use with this maximum permissible tissue concentration is the value of 23,000 for muscle of brook trout. Thus the freshwater Final Residue Value is (1.0 mg/kg)/23,000 = 0.000043 mg/kg or 0.043 μg/l. This value, however, probably should be lower. At this concentration half of the exposed brook trout would have concentrations which would exceed the FDA action level. Also the BCF of 63,000 for the fathead minnow is cause for concern. McKim et al. (1976) found that the concentration of mercury in muscle was equal to or greater than the whole body concentration. Also, Huckabee, et al. (1974) found that all fishes in a particular environment acquired about the same concentrations of mercury in both whole body and muscle tissue when they were chronically exposed to low concentrations of mercury. Thus the BCF for the edible portion of some consumed species may be equal to or higher than 63,000.

Information on the bioconcentration of various mercury compounds by saltwater animals is included in Table 5 and by saltwater plankton in Table 6. For mercuric chloride, bioconcentration factors ranged from 853 to 10,420 for algae. For the same compound the BCF values with animals ranged from 3.5 for the bloodworm to 10,000 for the oyster. In contrast, BCF values of 2,800, 40,000, and 40,000 were obtained with the oyster for mercuric acetate, methylmercuric chloride and phenylmercuric chloride, respectively.

To protect the marketability of shellfish for human consumption, Final Residue Values can be calculated based on the BCF values for the oyster and the FDA action level of 1.0 mg/kg. Accordingly, the Final Residue Values for mercury, based on data for mercuric chloride, mercuric acetate, methylmercuric chloride, and phenylmercuric chloride are 0.10, 0.36, 0.025, and 0.025 µg/l respectively. However, at these concentrations fifty percent of the exposed oysters would probably exceed the FDA action level.

Miscellaneous

Most of the significant freshwater and saltwater results in Table 6 have already been discussed in connection with data in Tables 1-5, but a few additional items deserve special mention. The data of Birge and Just (1973) illustrate life stage influences on sensitivity with four orders of magnitude difference in sensitivity between the embryonic and adult stages of the frog, Rana pipiens.

Another point of interest and possible considerable importance is the work of Heinz (1976) in which mallard ducks were fed food contaminated with methylmercuric dicyandiamide. These feeding studies extended over two generations and demonstrated reduced fertility and inhibited food conversion efficiency at a mercury concentration that was estimated to be equivalent to 0.1 mg/kg in the natural succulent food of the wild duck. These results were not used to estimate a Final Residue Value based on food for wildlife because the dicyandiamide compound may not represent the toxicity of methylmercury alone.

Summary

Freshwater acute data for divalent inorganic mercury span nine taxonomic orders from rotifers to fish. These acute values range from 0.02 to 2,000 µg/l and the Final Acute Value is 0.0017 µg/l. Acute values for methylmercury and other mercury compounds are only available for fishes; consequently an estimate of the range of species sensitivity for these compounds is not possible. However, methylmercuric chloride is about ten times more toxic to rainbow trout than mercuric chloride.

Available chronic data indicate that the methylmercury is the most chronically toxic of the tested mercury compounds, with the chronic values for Daphnia magna and brook trout being 1.00 and 0.52 µg/l, respectively. For inorganic mercury the chronic value obtained with Daphnia magna was about 1.6 and the acute-chronic ratio was 3.2.

Plant values indicate that they should be adequately protected by criteria derived to protect aquatic animals.

Based on the FDA action level of 1 mg/kg and a bioconcentration factor of 23,000 the Freshwater Final Residue Value is 0.043 µg/l. However, this concentration may not adequately protect the marketability of freshwater fish because, on the average, half of the individuals in a species such as brook trout will exceed the limit. In addition, data suggest that higher bioconcentration factors may be obtained with the edible portion of other consumed species.

Data on the acute toxicity of mercuric chloride are available for 26 species of saltwater animals including annelids, molluscs, crustaceans, echinoderms, and fishes. Species mean acute values range from 3.5 to 1,680 µg/l. Fishes are more resistant than average, whereas molluscs and crustaceans are more sensitive than average to the acute toxic effects of mercury. Concentrations of mercury that affected growth and photosynthetic activity of one saltwater diatom and six species of brown algae range from 10 to 160 µg/l.

Results of a life-cycle exposure with the mysid shrimp show that an inorganic mercury at a concentration of 1.6 µg/l significantly influenced time of appearance of first brood, time of first spawn, and productivity and the resulting acute-chronce ratio was 2.9.

A bioconcentration factor of 40,000 has been obtained for methylmercuric chloride with an oyster, which results in a Final Residue Value of 0.025 µg/l when used with the FDA action level. At this concentration, half of the oysters would exceed the action level.

For both freshwater and saltwater species many acute tests have been conducted on inorganic mercuric salts, but few acute tests have been conducted on other compounds of mercury. Although methylmercury is probably more acutely toxic than inorganic mercuric salts, few acute or chronic toxicity tests have been conducted on methylmercury and it apparently is removed from water rapidly. On the other hand, inorganic mercury is readily converted to methylmercury which can become a major residue problem in aquatic organisms.

CRITERIA

For total recoverable mercury the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.00057 µg/l as a 24-hour average, and the concentration should not exceed 0.0017 µg/l at any time.

For total recoverable mercury the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.025 µg/l as a 24-hour average, and the concentration should not exceed 3.7 µg/l at any time.

Table 1. Acute values for mercury

Species	Method*	Chemical	LC50/EC50** (µg/l)	Species Mean Acute Value** (µg/l)	Reference
		FRESHWATER SPECIES			
		Inorganic Mercuric Salts			
Rotifer, *Philodina acuticornis*	S, U	Mercuric chloride	518	-	Bulkema, et al. 1974
Rotifer, *Philodina acuticornis*	S, U	Mercuric chloride	1,185	784	Bulkema, et al. 1974
Bristleworm, *Nais* sp.	S, M	Mercuric nitrate	1,000	1,000	Rehwoldt, et al. 1973
Cladoceran, *Daphnia magna*	R, U	Mercuric chloride	5	5	Biesinger & Christensen, 1972
Scud, *Gammarus* sp.	S, M	Mercuric nitrate	10	10	Rehwoldt, et al. 1973
Crayfish (males only, mixed ages), *Faxonella cylpeatus*	R, M	Mercuric chloride	0.02	0.02	Heit & Fingerman, 1977
Crayfish, *Orconectes limosas*	S, M	Mercuric chloride	50	50	Boutet & Chaisemartin, 1973
Stonefly, *Acroneuria lycorius*	S, U	Mercuric chloride	2,000	2,000	Warnick & Bell, 1969
Mayfly, *Ephemerella subvaria*	S, U	Mercuric chloride	2,000	2,000	Warnick & Bell, 1969
Caddisfly, *Hydropsyche betteni*	S, U	Mercuric chloride	2,000	2,000	Warnick & Bell, 1969
Coho salmon (juvenile), *Oncorhynchus kisutsch*	S, M	Mercuric chloride	240	240	Lorz, et al. 1978
Rainbow trout (juvenile) *Salmo gairdneri*	FT, U	Mercuric chloride	400	-	MacLeod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	FT, U	Mercuric chloride	280	-	Macleod & Pessah, 1973

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50** (µg/l)	Species Mean Acute Value** (µg/l)	Reference
Rainbow trout (juvenile), *Salmo gairdneri*	FT, U	Mercuric chloride	220	-	Macleod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	R, U	Mercuric chloride	155	249	Matida, et al. 1971
		Methylmercuric Compounds			
Rainbow trout (larva), *Salmo gairdneri*	R, U	Methylmercuric chloride	24	-	Wobeser, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	R, U	Methylmercuric chloride	42	-	Wobeser, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	R, U	Methylmercuric chloride	25	29	Matida, et al. 1971
Brook trout (juvenile), *Salvelinus fontinalis*	FT, M	Methylmercuric chloride	84	-	McKim, et al. 1976
Brook trout (yearling), *Salvelinus fontinalis*	FT, M	Methylmercuric chloride	65	74	McKim, et al. 1976
		Other Mercury Compounds			
Rainbow trout (juvenile), *Salmo gairdneri*	R, U	Phenylmercuric acetate	5	5	Matida, et al. 1971
Goldfish, *Carassius auratus*	S, U	Phenylmercuric lactate	82	82	Ellis, 1947
Fathead minnow *Pimephales promelas*	R, M	Mercuric acetate	190	190	Curtis, et al. 1979
Fathead minnow *Pimephales promelas*	R, M	Mercuric thiocyanate	150	150	Curtis, et al. 1979
Channel catfish (juvenile), *Ictalurus punctatus*	S, U	Ethylmercuric phosphate	48***	48	Clemens & Sneed, 1959

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50** (µg/l)	Species Mean Acute Value** (µg/l)	Reference
Channel catfish (juvenile), Ictalurus punctatus	S, U	Ethylmercuric p-toluene sulfonanilide	51***	51	Clemens & Sneed, 1959
Channel catfish (juvenile), Ictalurus punctatus	S, U	Phenylmercuric acetate	35***	-	Clemens & Sneed, 1959
Channel catfish (juvenile), Ictalurus punctatus	S, U	Phenylmercuric acetate	1,158****	201	Clemens & Sneed, 1958
Channel catfish (juvenile), Ictalurus punctatus	S, U	Phenylmercuric acetate	<176*****	-	Clemens & Sneed, 1958
		SALTWATER SPECIES			
		Inorganic Mercuric Salts			
Polychaete (larva), Capitella capitata	S, U	Mercuric chloride	14	14	Reish, et al. 1976
Polychaete (adult), Neanthes arenaceodentata	S, U	Mercuric chloride	96	-	Reish, et al. 1976
Polychaete (juvenile), Neanthes arenaceodentata	S, U	Mercuric chloride	100	98	Reish, et al. 1976
Sandworm (adult), Nereis virens	S, U	Mercuric chloride	70	70	Eisler & Hennekey, 1977
Bay scallop (juvenile), Argopecten irradians	S, U	Mercuric chloride	89	89	Nelson, et al. 1976
Oyster, Crassostrea virginica	S, U	Mercuric chloride	5.6	-	Calabrese, et al. 1977
Oyster, Crassostrea virginica	S, U	Mercuric chloride	10.2	7.6	MacInnes & Calabrese, 1978
Oyster, Crassostrea gigas	S, M	Mercuric chloride	5.7	-	Glickstein, 1978

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50** (µg/l)	Species Mean Acute Value** (µg/l)	Reference
Oyster, *Crassostrea gigas*	S, M	Mercuric nitrate	5.5	5.6	Glickstein, 1978
Soft-shell clam (adult), *Mya arenaria*	S, U	Mercuric chloride	400	400	Eisler & Hennekey, 1977
Hard-shell clam, *Mercenaria mercenaria*	S, U	Mercuric chloride	4.8	4.8	Calabrese, et al. 1977
Clam (adult), *Rangia cuneata*	S, M	Mercuric chloride	58	-	Dillon, 1977
Clam (adult), *Rangia cuneata*	S, M	Mercuric chloride	122	84	Dillon, 1977
Copepod (adult), *Acartia tonsa*	S, U	Mercuric chloride	10	-	Sosnowski & Gentile, 1978
Copepod (adult), *Acartia tonsa*	S, U	Mercuric chloride	14	-	Sosnowski & Gentile, 1978
Copepod (adult), *Acartia tonsa*	S, U	Mercuric chloride	15	-	Sosnowski & Gentile, 1978
Copepod (adult), *Acartia tonsa*	S, U	Mercuric chloride	20	14	U.S. EPA, 1980
Copepod, *Acartia clausi*	S, U	Mercuric chloride	10	10	U.S. EPA, 1980
Copepod, *Eurytemora affinis*	S, U	Mercuric chloride	158	158	U.S. EPA, 1980
Copepod, *Nitocra spinipes*	S, U	Mercuric chloride	230	230	Bengtsson, 1978
Copepod, *Pseudodiaptomus coronatus*	S, U	Mercuric chloride	79	79	U.S. EPA, 1980

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50** (µg/l)	Species Mean Acute Value** (µg/l)	Reference
Copepod, *Tigriopus japonicus*	S, U	Mercuric chloride	223	223	U.S. EPA, 1980
Mysid shrimp, *Mysidopsis bahia*	FT, M	Mercuric chloride	3.5	3.5	U.S. EPA, 1980
Crab (larva), *Carcinus maenas*	S, U	Mercuric chloride	14	14	Connor, 1972
Crab (larva), *Cancer magister*	S, M	Mercuric chloride	6.6	6.6	Glickstein, 1978
Hermit crab (adult), *Pagurus longicarpus*	S, U	Mercuric chloride	50	50	Eisler & Hennekey, 1977
White shrimp (adult), *Penaeus setiferus*	S, U	Mercuric chloride	17	17	Green, et al. 1976
Starfish (adult), *Asterias forbesi*	S, U	Mercuric chloride	60	60	Eisler & Hennekey, 1977
Haddock (larva), *Melanogrammus aeglefinus*	S, U	Mercuric chloride	98	98	U.S. EPA, 1980
Mummichog (adult), *Fundulus heteroclitus*	S, U	Mercuric chloride	800	-	Eisler & Hennekey, 1977
Mummichog (adult), *Fundulus heteroclitus*	S, U	Mercuric chloride	2,000	1,260	Klaunig, et al. 1975
Fourspine stickleback (adult), *Apeltes quadracus apeltes*	S, U	Mercuric chloride	315	315	U.S. EPA, 1980
Atlantic silverside (larva), *Menidia menidia*	S, U	Mercuric chloride	144	-	U.S. EPA, 1980
Atlantic silverside (larva), *Menidia menidia*	S, U	Mercuric chloride	125	-	U.S. EPA, 1980

Table 1. (Continued)

Species	Method*	Chemical	LC50/EC50** (µg/l)	Species Mean Acute Value** (µg/l)	Reference
Atlantic silverside (juvenile), *Menidia menidia*	S, U	Mercuric chloride	86	116	U.S. EPA, 1980
Winter flounder (larva), *Pseudopleuronectes americanus*	S, U	Mercuric chloride	1,820	-	U.S. EPA, 1980
Winter flounder (larva), *Pseudopleuronectes americanus*	S, U	Mercuric chloride	1,560	-	U.S. EPA, 1980
Winter flounder (larva), *Pseudopleuronectes americanus*	S, U	Mercuric chloride	1,810	-	U.S. EPA, 1980
Winter flounder (larva), *Pseudopleuronectes americanus*	S, U	Mercuric chloride	1,320	-	U.S. EPA, 1980
Winter flounder (larva), *Pseudopleuronectes americanus*	S, U	Mercuric chloride	1,960	1,680	U.S. EPA, 1980
		Methylmercuric Compounds			
Amphipod (adult), *Gammarus duebeni*	S, U	Methylmercuric chloride	150	150	Lockwood & Inman, 1975
		Other Mercury Compounds			
Grass shrimp (adult), *Palaemonetes pugio*	S, M	Mercuric acetate	60	60	Curtis, et al. 1979
Grass shrimp (adult), *Palaemonetes pugio*	S, M	Mercuric thiocyanate	90	90	Curtis, et al. 1979

Table 1. (Continued)

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* S = static, R = renewal, FT = flow-through, U = unmeasured, M = measured.

** Results are expressed as mercury, not as the compound.

*** 19-20°C

**** 10°C

*****16.5 & 24°C

Table 2. Chronic values for mercury

Species	Test*	Chemical	Limits** (µg/l)	Chronic Value** (µg/l)	Reference
		FRESHWATER SPECIES			
		Inorganic Mercuric Salts			
Cladoceran, *Daphnia magna*	LC***	Mercuric chloride	1.3-2.7	1.87	Biesinger, et al. Manuscript
Cladoceran, *Daphnia magna*	LC****	Mercuric chloride	0.9-1.8	1.27	Biesinger, et al. Manuscript
		Methylmercuric Compounds			
Cladoceran, *Daphnia magna*	LC***	Methylmercuric chloride	<0.01-0.04	-*****	Biesinger, et al. Manuscript
Cladoceran, *Daphnia magna*	LC****	Methylmercuric chloride	0.87-1.14	1.00	Biesinger, et al. Manuscript
Brook trout, *Salvelinus fontinalis*	LC	Methylmercuric chloride	0.29-0.93	0.52	McKim, et al. 1976.
		Other Mercury Compounds			
Cladoceran, *Daphnia magna*	LC****	Phenylmercuric acetate	1.90-3.20	2.47	Biesinger, et al. Manuscript
		SALTWATER SPECIES			
		Inorganic Mercuric Salts			
Mysid shrimp, *Mysidopsis bahia*	LC	Mercuric chloride	0.82-1.65	1.2	U.S. EPA, 1980

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* LC = partial life cycle or full life cycle.

** Results are expressed as mercury, not as the compound.

*** Flow-through

**** Renewal

*****Chronic value cannot be calculated because the lower limit is a "less than" value.

Table 2. (Continued)

		Acute-Chronic Ratio		
Species	Chemical	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
		Inorganic Mercury		
Cladoceran, *Daphnia magna*	Mercuric chloride	5	1.87	2.7
Cladoceran, *Daphnia magna*	Mercuric chloride	5	1.27	3.9
Mysid shrimp, *Mysidopsis bahia*	Mercuric chloride	3.5	1.2	2.9
		Methylmercuric Compounds		
Brook trout *Salvelinus fontinalis*	Methylmercuric chloride	74	0.52	140

Table 3. Species mean acute values and acute-chronic ratios for mercury

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	FRESHWATER SPECIES		
	Inorganic Mercuric Salts		
11	Caddisfly, *Hydropsyche betteni*	2,000	-
10	Stonefly, *Acroneuria lycorias*	2,000	-
9	Mayfly, *Ephemerella subvaria*	2,000	-
8	Bristleworm, *Nais* sp.	1,000	-
7	Rotifer, *Philodina acuticornis*	784	-
6	Rainbow trout, *Salmo gairdneri*	249	-
5	Coho salmon, *Oncorhynchus kisutch*	240	-
4	Crayfish, *Orconectes limosus*	50	-
3	Scud, *Gammarus* sp.	10	-
2	Cladoceran, *Daphnia magna*	5	3.2
1	Crayfish, *Faxonella clypeata*	0.02	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	SALTWATER SPECIES		
	Inorganic Mercuric Salts		
26	Winter flounder, *Pseudopleuronectes americanus*	1,680	-
25	Mummichog, *Fundulus heteroclitus*	1,260	-
24	Soft-shell clam, *Mya arenaria*	400	-
23	Fourspine stickleback, *Apeltes quadracus*	315	-
22	Copepod, *Nitocra spinipes*	230	-
21	Copepod, *Tigriopus japonicus*	223	-
20	Copepod, *Eurytemora affinis*	158	-
19	Atlantic silverside, *Menidia menidia*	116	-
18	Haddock, *Melanogrammus aeglefinus*	98	-
17	Polychaete, *Neanthes arenaceodentata*	98	-
16	Bay scallop, *Argopecten irradians*	89	-
15	Clam, *Rangia cuneata*	84	-
14	Copepod, *Pseudodiaptomus coronatus*	79	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
13	Sandworm, *Nereis virens*	70	-
12	Starfish, *Asterias forbesi*	60	-
11	Hermit crab, *Pagurus longicarpus*	50	-
10	White shrimp, *Penaeus setiferus*	17	-
9	Copepod, *Acartia tonsa*	14	-
8	Polychaete, *Capitella capitata*	14	-
7	Crab, *Carcinus maenas*	14	-
6	Copepod, *Acartia clausi*	10	-
5	Oyster, *Crassostrea virginica*	7.6	-
4	Crab, *Cancer magister*	6.6	-
3	Oyster, *Crassostrea gigas*	5.6	-
2	Hard-shell clam, *Mercenaria mercenaria*	4.8	-
1	Mysid shrimp, *Mysidopsis bahia*	3.5	2.9

Table 3. (Continued)

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* Ranked from least sensitive to most sensitive based on species mean acute value.

Inorganic mercuric salts

Freshwater Final Acute Value = 0.0017 µg/l

Saltwater Final Acute Value = 3.71 µg/l

Final Acute-Chronic Ratio = 3.0

Freshwater Final Chronic Value = (0.0017 µg/l)/3.0 = 0.00057 µg/l

Saltwater Final Chronic Value = (3.71 µg/l)/3.0 = 1.2 µg/l

Table 4. Plant values for mercury

Species	Chemical	Effect	Result* (µg/l)	Reference
FRESHWATER SPECIES				
Inorganic Mercuric Salts				
Alga, *Chlorella vulgaris*	Mercuric chloride	32-day EC50, cell division inhibition	1,030	Rosko & Rachlin, 1977
Water milfoil, *Myriophyllum spicatum*	Mercuric chloride	32-day EC50, root growth inhibition	1,200	Stanley, 1974
SALTWATER SPECIES				
Inorganic Mercuric Salts				
Seaweed, *Ascophyllum nodosum*	Mercuric chloride	10-day EC50, growth	100	Stromgren, 1980
Diatom, *Ditylum brightwellii*	Mercuric chloride	10-day EC50, growth	10	Canterford & Canterford, 1980
Seaweed, *Fucus serratus*	Mercuric chloride	10-day EC50, growth	160	Stromgren, 1980
Seaweed, *Fucus spiralis*	Mercuric chloride	10-day EC50, growth	80	Stromgren, 1980
Seaweed, *Fucus vesiculosus*	Mercuric chloride	10-day EC50, growth	45	Stromgren, 1980
Giant kelp, *Macrocystis pyrifera*	Mercuric chloride	10-day EC50, growth	50	Clendenning & North, 1959
Seaweed, *Pelvetia canaliculata*	Mercuric chloride	10-day EC50, growth	130	Stromgren, 1980

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* Results are expressed as mercury, not as the compound

Table 5. Residues for mercury

Species	Tissue	Chemical	Bioconcentration Factor	Duration (days)	Reference
		FRESHWATER SPECIES			
		Methylmercuric Compounds			
Brook trout, Salvelinus fontinalis	muscle	Methylmercuric chloride	23,000	273	McKim, et al. 1976
Brook trout, Salvelinus fontinalis	whole fish	Methylmercuric chloride	15,000	273	McKim, et al. 1976
Brook trout, Salvelinus fontinalis	muscle or whole fish	Methylmercuric chloride	12,000	756	McKim, et al. 1976
Fathead minnow, Pimephales promelas	whole fish	methylmercuric chloride	63,000	336	Olson, et al. 1975
		SALTWATER SPECIES			
		Inorganic Mercuric Salts			
Blood worm, Glycera dibranchiata	Whole animal	Mercuric chloride	3.5	3	Medeiros, et al. 1980
Lobster (adult), Homarus americanus	Tail muscle	Mercuric chloride	129	30	Thurberg, et al. 1977
Oyster (adult), Crassostrea virginica	Soft parts	Mercuric chloride	10,000	74	Kopfler, 1974
		Methylmercuric compounds			
Oyster (adult), Crassostrea virginica	Soft parts	Methylmercuric chloride	40,000	74	Kopfler, 1974
		Other Mercury Compounds			
Oyster (adult), Crassostrea virginica	Soft parts	Phenylmercuric chloride	40,000	74	Kopfler, 1974
Oyster (adult), Crassostrea virginica	Soft parts	Mercuric acetate	2,800	45	Cunningham & Tripp, 1973

Table 5. (Continued)

	Maximum Permissible Tissue Concentration		
Species	Action Level or Effect	Concentration (mg/kg)	References
Man	edible fish or shellfish	1.0	U.S. FDA Guideline 7408.09, 1978
Mink, *Mustela vison*	histological evidence of injury	1.1	Wobeser, 1973
Brook trout, *Salvelinus fontinalis*	death (700 days)	5-7	McKim, et al. 1976

Methylmercury:

Freshwater Final Residue Value = (1.0 mg/kg)/23,000 = 0.000043 mg/l = 0.043 µg/l

Saltwater Final Residue Value = (1.0 mg/kg)/40,000 = 0.000025 mg/l = 0.025 µg/l

Table 6. Other data for mercury

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
		FRESHWATER SPECIES			
		RESIDUE DATA			
		Inorganic Mercuric Salts			
Alga, *Synedra ulna*	Mercuric chloride	0.29 days	BCF=29,000	0.25	Fujita & Hashizume, 1972
		Methylmercuric Compounds			
Alga, *Scenedesmus obliquus*	Methylmercuric chloride	14 days	BCF=761-2,100 (Maximum by third day)	60**	Havlik, et al. 1979
Alga, *Microcystis incerta*	Methylmercuric chloride	14 days	BCF=461-990 (Maximum by third day)	60**	Havlik, et al. 1979
Rainbow trout (juvenile), *Salmo gairdneri*	Methylmercuric chloride	84 days***	BCF=4,530 (whole fish)	0.263, at 5 C	Reinert, et al. 1974
Rainbow trout (juvenile), *Salmo gairdneri*	Methylmercuric chloride	84 days***	BCF=6,620 (whole fish)	0.258 at 10 C	Reinert, et al. 1974
Rainbow trout (juvenile), *Salmo gairdneri*	Methylmercuric chloride	84 days***	BCF=8,049 (whole fish)	0.234 at 15 C	Reinert, et al. 1974
Bluegill (juvenile), *Lepomis macrochirus*	Methylmercuric chloride	28.5 days	BCF=373 (whole fish)	0.2****-0.5 at 9 C	Cember, et al. 1978
Bluegill (juvenile), *Lepomis macrochirus*	Methylmercuric chloride	28.5 days	BCF=921 (whole fish)	0.5****-5.0 at 21 C	Cember, et al. 1978
Bluegill (juvenile), *Lepomis macrochirus*	Methylmercuric chloride	28.5 days	BCF=2,400 (whole fish)	0.2****-5.0, at 33 C	Cember, et al. 1978

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Mosquitofish, *Gambusia affinis*	Methylmercuric chloride	30 days	BCF=2,500 (whole fish)	0.8 µg/l water, at 10°C	Boudou, et al. 1979
Mosquitofish, *Gambusia affinis*	Methylmercuric chloride	30 days	BCF=4,300 (whole fish)	0.8 µg/l water, at 18°C	Boudou, et al. 1979
Mosquitofish, *Gambusia affinis*	Methylmercuric chloride	30 days	BCF=3,000 (whole fish)	0.8 µg/l water, 164 mg/kg food, 10°C	Boudou, et al. 1979
Mosquitofish, *Gambusia affinis*	Methylmercuric chloride	30 days	BCF=27,000 (whole fish)	0.8 µg/l water, 238 mg/kg food, 26°C	Boudou, et al. 1979
			Other Mercury Compounds		
Alga, *Scenedesmus obliquus*	Phenylmercuric chloride	14 days	BCF=553-1,300 (Maximum by third day)	60	Havlik, et al. 1979
Alga, *Microcystis incerta*	Phenylmercuric chloride	14 days	BCF=252-400 (Maximum by third day)	60	Havlik, et al. 1979
			NON-RESIDUE DATA		
			Inorganic Mercuric Salts		
Alga, Spring assemblages (predominantely diatoms)	Mercuric chloride	2 hrs	Photosynthetic activity EC50	80	Blinn, et al. 1977
Alga, *Ankistrodesmus braunii*	Mercuric chloride	336 hrs	Lipid biosynthesis inhibition EC50	2,590	Matson, et al. 1972
Alga, *Euglena gracilis*	Mercuric chloride	240-336 hrs	Lipid biosynthesis inhibition <EC50	2,590	Matson, et al. 1972
Sludge worm, *Tubifex tubifex*	Mercuric chloride	48 hrs	LC50	82	Brkovic-Popovic & Popovic, 1977a

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Sludge worm, *Tubifex tubifex*	Mercuric chloride	48 hrs	LC50	100	Brkovic-Popovic & Popovic, 1977b
Snail (embryo), *Amnicola* sp.	Mercuric nitrate	96 hrs	LC50	2,100	Rehwoldt, et al. 1973
Snail (adult) *Amnicola* sp.	Mercuric nitrate	96 hrs	LC50	80	Rehwoldt, et al. 1973
Cladoceran, *Daphnia magna*	Mercuric nitrate	Life cycle	LC50	4.8	Biesinger & Christensen, 1972
Crayfish (mixed ages, males only), *Faxonella clypeatus*	Mercuric nitrate	72 hrs	LC50	0.2	Heit & Fingerman, 1977
Crayfish (mixed ages, males only), *Procambarus clarki*	Mercuric nitrate	72 hrs	LC50	0.2	Heit & Fingerman, 1977
Crayfish (0.2 g), *Procambarus clarki*	Mercuric nitrate	24 hrs	LC50	10	Heit & Fingerman, 1977
Crayfish (1.2 g), *Procambarus clarki*	Mercuric nitrate	672 hrs	LC50	10	Heit & Fingerman, 1977
Crayfish (adult), *Orconectes limosus*	Mercuric chloride	96 hrs	LC60	740	Doyle, et al. 1976
Crayfish (juvenile), *Orconectes limosus*	Mercuric chloride	30 days	LC50 (unfed)	2	Boutet & Chaisemartin, 1973
Crayfish (juvenile), *Orconectes limosus*	Mercuric chloride	30 days	LC50 (fed)	<2	Boutet & Chaisemartin, 1973
Midge, *Chironomus* sp.	Mercuric nitrate	96 hrs	LC50	20	Rehwoldt, et al. 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result (µg/l)	Reference
Freshwater community (preliminary producers, herbivores and carnivorous midges)	Mercuric chloride	1 yr	Reduced algal numbers, standing stock, and diversity, numbers of species, evenness of distribution; no evicance of significant effects on midges	≥0.1	Sigmon, et al. 1977
Pink salmon (embryo), Oncorhynchus gorbuscha	Mercuric sulfate	2 days <time from fertilization to hatch	EC32 to EC81	5.2	Servizi & Martens, 1978
Pink salmon (pre-eyed embryo), Oncorhynchus gorbuscha	Mercuric sulfate	2 days <time from fertilization to stage	LC100	8.5	Servizi & Martens, 1978
Pink salmon (larva), Oncorhynchus gorbuscha	Mercuric sulfate	168 hrs	LC50	140	Servizi & Martens, 1978
Sockeye salmon (embryo), Oncorhynchus nerka	Mercuric sulfate	2 days <time from fertilization to hatch	EC45.6	4.3	Servizi & Martens, 1978
Sockeye salmon (pre-eyed embryo), Oncorhynchus nerka	Mercuric sulfate	2 days <time from fertilization to stage	LC100	9.3	Servizi & Martens, 1978
Sockeye salmon (larva), Oncorhynchus nerka	Mercuric sulfate	168 hrs	LC50	290	Servizi & Martens, 1978
Sockeye salmon (juvenile), Oncorhynchus nerka	Mercuric sulfate	168 hrs	LC50	190	Servizi & Martens,
Rainbow trout (juvenile), Salmo gairdneri	Mercuric chloride	24 hrs	LC50	903	Wobesor, 1973
Rainbow trout (juvenile), Salmo gairdneri	Mercuric chloride	2 hrs	Depressed olfactory bulbar response	74	Hara, et al. 1976
Rainbow trout (juvenile), Salmo gairdneri	Mercuric chloride	≥64 days	Growth	>21	Matida, et al. 1971

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Brook trout, *Salvelinus fontinalis*	Mercuric chloride	48 hrs	Increased cough frequency	≥3	Drummond, et al. 1974
Carp (embryo), *Cyprinus carpio*	Mercuric chloride	60-72 hrs	Reduced hatching success	≥3,000	Huckabee & Griffith, 1974
White sucker (adult), *Catostomus commersoni*	Mercuric chloride	6 min	Blood enzyme (LDH) inhibition 20%	8,000	Christensen, 1972
White sucker (adult), *Catostomus commersoni*	Mercuric chloride	16 min	Blood enzyme (GOT) inhibition 20%	10,000	Christensen, 1972
Threespine stickleback, *Gasterosteus aculeatus*	Mercuric chloride	10 days	LC0	>8	Jones, 1939
Threespine stickleback, *Gasterosteus aculeatus*	Mercuric chloride	110 min	Death	4,020	Jones, 1947
Mosquitofish, *Gambusia affinis*	Mercuric chloride	>10 days	LC50	500	Boudou, et al. 1979
Leopard frog (cleavage embryo), *Rana pipiens*	Mercuric chloride	96 hrs	LC50	>1.0-<10	Birge & Just, 1973
Leopard frog (blastula embryo), *Rana pipiens*	Mercuric chloride	96 hrs	LC50	>1.0-<10	Birge & Just, 1973
Leopard frog (gastrula embryo), *Rana pipiens*	Mercuric chloride	96 hrs	LC50	>1.0-<10	Birge & Just, 1973
Leopard frog (neurula embryo), *Rana pipiens*	Mercuric chloride	96 hrs	LC50	>0.1-<10	Birge & Just, 1973
Leopard frog (tail bud embryo), *Rana pipiens*	Mercuric chloride	96 hrs	LC50	>0.1-<10	Birge & Just, 1973
Leopard frog (larva), *Rana pipiens*	Mercuric chloride	5 days	LC50	1,000	Birge & Just, 1973
Leopard frog (adult), *Rana pipiens*	Mercuric chloride	96 hrs	LC50	>7,500-<10,000	Birge & Just, 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
			Methylmercuric Compounds		
Alga, *Ankistrodesmus braunii*	Methylmercuric chloride	336 hrs	Lipid biosynthesis, >EC50	1,598	Matson, et al. 1972
Alga, *Coelastrum microporum*	Methylmercuric chloride	Not stated	Growth inhibition, EC50	>2.4-<4.8	Holderness, et al. 1975
Rainbow trout, *Salmo gairdneri*	Methylmercuric chloride	$\geq$64 days	Growth inhibition	$\geq$0.04	Matida, et al. 1971
Rainbow trout, *Salmo gairdneri*	Methylmercuric chloride	120 days	Loss of appetite (as µg of Hg in total ration consumed, 1/3 as CH_3HgCl)	860	Matida, et al. 1971
Rainbow trout, *Salmo gairdneri*	Methylmercuric chloride	269 days	Loss of nervous control (as µg/l of Hg in total ration of consumed, 1/3 as CH_3HgCl)	1,600	Matida, et al. 1971
Rainbow trout, *Salmo gairdneri*	Methylmercuric chloride	30 min	Reduced viability of sperm - EC50	1,000	McIntyre, 1973
Brook trout (embryo), *Salvelinus fontinalis*	Methylmercuric chloride	16-17 days	Decreased enzyme (GOT) activity	0.88	Christensen, 1975
Brook trout (alevin), *Salvelinus fontinalis*	Methylmercuric chloride	Incubation period + 21 days	Reduced growth	0.79	Christensen, 1975
Brook trout (alevins), *Salvelinus fontinalis*	Methylmercuric chloride	30 days	Increased enzyme (GOT) activity	0.79	Christensen, 1975
Brook trout (juvenile), *Salvelinus fontinalis*	Methylmercuric chloride	14 days	Increased blood plasma chloride	2.93	Christensen, et al. 1977
Brook trout, *Salvelinus fontinalis*	Methylmercuric chloride	8 days	Increased cough frequency	$\geq$3	Drummond, et al. 1974
Mosquitofish, *Gambusia affinis*	Methylmercuric chloride	<24 hrs	LC50	500	Boudou, et al. 1979

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Newt, *Triturus viridescens*	Methylmercuric chloride	≥2 days	Delayed limb regeneration	8	Chang, et al. 1976
Newt, *Triturus viridescens*	Methylmercuric chloride	17 days	Death	24	Chang, et al. 1976
Newt, *Triturus viridescens*	Methylmercuric chorlde	8 days	Death	8	Chang, et al. 1976
Leopard frog (tadpole), *Rana pipiens*	Methylmercuric chloride	48 hrs	LC100	50	Chang, et al. 1974
Leopard frog, *Rana pipiens*	Methylmercuric chloride	≤4 mos	Failure to metamorphose	1	Chang, et al. 1974
Leopard frog (blastula embryo), *Rana pipiens*	Methylmercuric chloride	5 days	LC50	12-16	Dial, 1976
Leopard frog (gastrula embryo), *Rana pipiens*	Methylmercuric chloride	5 days	LC50	8-12	Dial, 1976
Leopard frog (neural plate embryo), *Rana pipiens*	Methylmercuric chloride	5 days	LC50	12-16	Dial, 1976
Leopard frog (blastula embryo), *Rana pipiens*	Methylmercuric chloride	96 hrs	Teratogenesis EC50	4-8	Dial, 1976
Leopard frog (gastrula embryo), *Rana pipiens*	Methylmercuric chloride	96 hrs	Teratogenesis EC50	12-16	Dial, 1976
Leopard frog (neural plate embryo), *Rana pipiens*	Methylmercuric chloride	96 hrs	Teratogenesis EC50	12-24	Dial, 1976
Mink (adult), *Mustela vison*	Methylmercuric chloride	93 days	Histologic evidence of injury	1,100	Wobeser, 1973
Mink (adult), *Mustola vison*	Methylmercuric chloride	93 days	LC50 in brain tissue	11,000	Wobeser, 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
	Other Mercury Compounds				
Alga, Florida Lake assemblage	Methylmercuric dicyandiamide	24 hrs	Growth of population inhibition	≤0.8	Harriss, et al. 1970
Alga, Florida Lake assemblage	N-Methylmercuric-1,2,3,6-tetrahydro-3,6-methano-3,4,5,6,7,7,-hexachloro-phthalimide	24 hrs	Growth of population inhibition	≤0.3	Harriss, et al. 1970
Alga, Cladophoraceae	Ethylmercuric phosphate	1 hr	Nuisance control	38.6	Burrows & Combs, 1958
Alga, Ulothrichaceae	Ethylmercuric phosphate	1 hr	Nuisance control	38.6	Burrows & Combs, 1958
Alga, Florida Lake assemblage	Phenylmercuric acetate	24 hrs	Growth of population inhibition	≤0.6	Harriss, et al. 1970
Alga, Florida Lake assemblage	Diphenyl mercury	24 hrs	Growth of population inhibition	≤28.3	Harriss, et al. 1970
Louisiana red crayfish (juvenile), *Procambarus clarki*	Methylmercuric dicyandimide	110 hrs	LC50	53.6	Hendrick & Everett, 1965
Chinook salmon (fingerling), *Oncorhynchus tshawytscha*	Ethylmercuric phosphate	1 hr	Distress	77	Burrows & Combs, 1958
Chinook salmon, *Oncorhynchus tshawsytscha*	Ethylmercuric phosphate	20 hrs	Safe for disease control	39	Burrows & Combs, 1958
Sockeye salmon (juvenile), *Oncorhynchus nerka*	Pyridylmercuric acetate	1.5 hrs	LC50	10,600-15,800	Burrows & Palmer, 1949
Sockeye salmon (juvenile), *Oncorhynchus nerka*	Pyridylmercuric acetate	1.5 hrs	Safe for disease control	≤954	Rucker, 1948
Sockeye salmon (juvenile), *Oncorhynchus nerka*	Pyridylmercuric acetate	1 hr	Safe for disease control	<4,752	Rucker & Whipple, 1951

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Rainbow trout (juvenile), *Salmo gairdneri*	Pyridylmercuric acetate	1 hr	LC100	1,030	Allison, 1957
Rainbow trout (juvenile), *Salmo gairdneri*	Pyridylmercuric acetate	1 hr	LC0	967	Allison, 1957
Rainbow trout (juvenile), *Salmo gairdneri*	Pyridylmercuric acetate	1 hr	LC50	4,750	Rodgers, et al. 1951
Rainbow trout (juvenile), *Salmo gairdneri*	Pyridylmercuric acetate	1 hr	LC18	2,380	Rodgers, et al. 1951
Rainbow trout (alevin), *Salmo gairdneri*	Pyridylmercuric acetate	1 hr	Safe for disease control	≤4,750	Rucker & Whipple, 1951
Rainbow trout (juvenile), *Salmo gairdneri*	Pyridylmercuric acetate	1 hr	LC60	517	Allison, 1957
Rainbow trout, *Salmo gairdneri*	Phenylmercuric acetate	≥64 days	Growth	0.11-1.1	Matida, et al. 1971
Rainbow trout (juvenile) *Salmo gairdneri*	Ethylmercuric phosphate	48 hrs	LC50	43	Matida, et al. 1971
Rainbow trout (juvenile) *Salmo gairdneri*	Ethylmercuric p-toluene sulfonanilide	-	Retarded learning	5 µg/g in feed daily or 10 µg/g feed every fifth day	Hartman, 1978
Rainbow trout (juvenile), *Salmo gairdneri*	Phenylmercuric acetate	24 hrs	LC50	25	MacLeod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	Phenylmercuric acetate	48 hrs	LC50	1,780	Willford, 1967
Rainbow trout (juvenile), *Salmo gairdneri*	Merthiolate	48 hrs	LC50	10,500	Willford, 1967
Rainbow trout (juvenile), *Salmo gairdneri*	Mercurous nitrate	96 hrs	LC50	33	Hale, 1977

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Brown trout (juvenile), *Salmo trutta*	Phenylmercuric acetate	1 hr	Safe for disease	4,750	Rodgers, et al. 1951
Brown trout (juvenile), *Salmo trutta*	Pyridylmercuric acetate	48 hrs	LC50	2,950	Willford, 1967
Brown trout (juvenile), *Salmo trutta*	Merthiolate	48 hrs	LC50	26,800	Willford, 1967
Brook trout (juvenile), *Salvelinus fontinalis*	Phenylmercuric acetate	1 hr	Safe for disease control	2,070	Allison, 1957
Brook trout (juvenile), *Salvelinus fontinalis*	Phenylmercuric acetate	1 hr	Safe for disease control	4,750	Rodgers, et al. 1951
Brook trout (juvenile), *Salvelinus fontinalis*	Pyridylmercuric acetate	48 hrs	LC50	5,080	Willford, 1967
Brook trout (juvenile), *Salvelinus fontinalis*	Merthiolate	48 hrs	LC50	39,900	Willford, 1967
Lake trout (juvenile), *Salvelinus namaycush*	Pyridylmercuric acetate	48 hrs	LC50	3,610	Willford, 1967
Lake trout (juvenile), *Salvelinus namaycush*	Merthiolate	48 hrs	LC50	1,060	Willford, 1967
Channel catfish (juvenile), *Ictalurus punctatus*	Phenylmercuric acetate	48 hrs	LC50 @ 10°C	1,960	Clements & Sneed, 1958
Channel catfish (juvenile), *Ictalurus punctatus*	Phenylmercuric acetate	48 hrs	LC50 @ 16.5°C	1,360	Clemens & Sneed, 1958
Channel catfish (juvenile), *Ictalurus punctatus*	Phenylmercuric acetate	48 hrs	LC50 @ 24°C	233	Clemens & Sneed, 1958
Channel catfish (yolk sac fry), *Ictalurus punctatus*	Phenylmercuric acetate	48 hrs	LC50 @ 24°C	178	Clemens & Sneed, 1958
Channel catfish (1 wk-old), *Ictalurus punctatus*	Phenylmercuric acetate	24 hrs	LC50 @ 23°C	1,040	Clemens & Sneed, 1958

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Channel catfish (juvenile 3"), Ictalurus punctatus	Phenylmercuric acetate	24 hrs	LC50 @ 23°C	1,780	Clemens & Snead, 1958
Channel catfish, Ictalurus punctatus	Phenylmercuric acetate	48 hrs	LC50	1,370	Willford, 1967
Channel catfish, Ictalurus punctatus	Merthiolate	48 hrs	LC50	2,800	Willford, 1967
Bluegill (juvenile), Lepomis macrochirus	Pyridylmercuric acetate	48 hrs	LC50	7,600	Willford, 1967
Bluegill (juvenile), Lepomis macrochirus	Merthiolate	48 hrs	LC50	32,000	Willford, 1967
Mallard duck, Anas platyrhynchos	Methylmercuric dicyandiamide	2 generations	Reduced fertility and food conversion efficiency	0.1 mg/kg in food	Heinz, 1976
			SALTWATER SPECIES		
			Inorganic Mercuric Salts		
Red alga, Antithamnion plumula	Mercuric chloride	30 min	LC50 after 7 days	5,000	Boney & Corner, 1959
Alga, Chaetoceros glavestonensis	Mercuric chloride	4 days	About 30% reduction in growth	10	Hannan, et al. 1973b
Alga, Chaetoceros galvestonensis	Mercuric chloride	4 days	No growth of culture	100	Hannan, et al. 1973b
Alga, Chaetoceros galvestonensis	Mercuric chloride	4 days	BCF=10,920	10	Hannan, et al. 1973b
Alga, Chlorella sp.	Mercuric chloride	-	66% reduction in CO_2	2,500	Mills & Colwell, 1977
Alga, Croomonas salina	Mercuric chloride	2 days	BCF=853	164	Parrish & Carr, 1976
Alga, Cyclotella sp.	Mercuric chloride	3 days	No growth of culture	100	Hannan & Patoulliet, 1972

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Alga, *Dunaliella* sp.	Mercuric chloride	-	75% reduction in CO_2	2,500	Mills & Colwell, 1977
Alga, *Dunaliella tertiolecta*	Mercuric chloride	8 days	About 10% increase in maximum chlorophyll *a* concentration	100	Betz, 1977
Alga, *Dunaliella tertiolecta*	Mercuric chloride	8 days	About 45% increase in maximum chlorophyll *a* concentration	220	Betz, 1977
Alga, *Dunaliella tertiolecta*	Mercuric chloride	3 days	About 15% reduction in growth	10	Davies, 1976
Alga, *Dunaliella tertiolecta*	Mercuric chloride	8 days	No effect on growth	2	Davies, 1976
Alga, *Isochrysis galbana*	Mercuric chloride	15 days	About 10% reduction in growth	5.1	Davies, 1974
Alga, *Isochrysis galbana*	Mercuric chloride	15 days	About 60% reduction in growth	10.5	Davies, 1974
Alga, *Isochrysis galbana*	Mercuric chloride	28 days	Growth rate recover to near normal after day 5	10.5	Davies, 1974
Kelp (zoospores, gametophytes, sporophytes), *Laminaria hyperborea*	Mercuric chloride	28 days	Lowest concentration for growth inhibition	10	Hopkins & Kain, 1971
Kelp (zoospores, gametophytes, sporophytes), *Laminaria hyperborea*	Mercuric chloride	22 hrs	EC50 respiration	about 450	Hopkins & Kain, 1971
Kelp (zoospores, gametophytes, sporophytes), *Laminaria hyperborea*	Mercuric chloride	28 days	About 80% reduction in respiration	10,000	Hopkins & Kain, 1971

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Alga, *Phaeodactylum tricornutum*	Mercuric chloride	4 days	About 50% reduction in growth	50	Hannan, et al. 1973b
Alga, *Phaeodactylum tricornutum*	Mercuric chloride	4 days	No growth of culture	120	Hannan, et al. 1973a
Alga, *Phaeodactylum tricornutum*	Mercuric chloride	4 days	BCF=7,120	10	Hannan, et al. 1973b
Red alga (sporling), *Plumaria elegans*	Mercuric chloride	24 hrs	40% reduction in growth over 21 days	120	Boney, 1971
Red alga (sporling), *Plumaria elegans*	Mercuric chloride	1 hr	40% reduction in growth over 21 days	1,000	Boney, 1971
Red alga (sporling), *Plumaria elegans*	Mercuric chloride	18 hrs	LC50 after 7 days	3,170	Boney, et al. 1959
Red alga, *Plumaria elegans*	Mercuric chloride	30 min	LC50 after 7 days	6,700	Boney & Corner, 1959
Red alga, *Polysiphonia lanosa*	Mercuric chloride	30 min	LC50 after 7 days	8,000	Boney & Corner, 1959
Alga (mixed), *Asterionella japonica* plus *Diogenes* sp.	Mercuric chloride	8 days	BCF=3,467	15	Laumond, et al. 1973
5 seaweed species, *Ascophyllum nodosum*, *Fucus spiralis*, *F. versiculosus*, *F. serratus*, *Pelvetia canaliculata*	Mercuric chloride	10 days	10-30% reduction in growth	10	Stromgren, 1980
Algae, 18 species	Mercuric chloride	17 days	Growth inhibition	<5-15	Berland, et al. 1976
Algae, 18 species	Mercuric chloride	17 days	Lethal	10-50	Berland, et al. 1976
Algae, (three species)	Mercuric chloride	-	Depressed growth	30-350	Sick & Windom, 1975

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Algae, (three species)	Mercuric chloride	-	No further bioaccumulation	40	Sick & Windom, 1975
Algae, (three species)	Mercuric chloride	-	Changes in cell chemistry	30-350	Sick & Windom, 1975
Sandworm (adult), *Nereis virens*	Mercuric chloride	168 hrs	LC50	60	Eisler & Hennekey, 1977
Sandworm (adult), *Nereis virens*	Mercuric chloride	168 hrs	LC100	125	Eisler & Hennekey, 1977
Polychaete (adult), *Ophryotrocha diadema*	Mercuric chloride	96 hrs	LC13	50	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha diadema*	Mercuric chloride	96 hrs	LC60	100	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha diadema*	Mercuric chloride	96 hrs	LC100	500	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha diadema*	Mercuric chloride	21 days	No growth of population	100	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha labronica*	Mercuric chloride	0.5 hrs	LC50	1,000	Brown & Ahsanullah, 1971
Oyster (larva), *Crassostrea gigas*	Mercuric chloride	24 hrs	Abnormal development	32	Okubo & Okubo, 1962
Oyster (embryo), *Crassostrea virginica*	Mercuric chloride	12 days	LC5	3.3	Calabrese, et al. 1977
Oyster (embryo), *Crassostrea virginica*	Mercuric chloride	12 days	LC50	12	Calabrese, et al. 1977
Oyster (embryo), *Crassostrea virginica*	Mercuric chloride	12 days	LC95	20	Calabrese, et al. 1977
Oyster (embryo), *Crassostrea virginica*	Mercuric chloride	48 hrs	LC0	1	Calabrese, et al. 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Oyster (adult), *Crassostrea virginica*	Mercuric chloride	19 days	Trace metal upset	50	Kopfler, 1974
Hard-shell clam (larva), *Mercenaria mercenaria*	Mercuric chloride	8-10 days	LC5	4	Calabrese, et al. 1977
Hard-shell clam (larva), *Mercenaria mercenaria*	Mercuric chloride	8-10 days	LC50	14	Calabrese, et al. 1977
Hard-shell clam (larva), *Mercenaria mercenaria*	Mercuric chloride	8-10 days	LC95	25	Calabrese, et al. 1977
Hard-shell clam (larva), *Mercenaria mercenaria*	Mercuric chloride	42-48 hrs	LC0	2.5	Calabrese, et al. 1973
Soft-shell clam (adult), *Mya arenaria*	Mercuric chloride	168 hrs	LC0	1	Eisler & Hennekey, 1977
Soft-shell clam (adult), *Mya arenaria*	Mercuric chloride	168 hrs	LC50	4	Eisler & Hennekey, 1977
Soft-shell clam (adult), *Mya arenaria*	Mercuric chloride	168 hrs	LC100	30	Eisler & Hennekey, 1977
Blue mussle (larva), *Mytilus edulis*	Mercuric chloride	24 hrs	Abnormal development	32	Okubo & Okubo, 1962
Clam, *Rangia cuneata*	Mercuric chloride	14 days	BCF=1,130 Whole animal	34	Dillon & Neff, 1978
Copepods (adult), 5 genera	Mercuric chloride	10 days	≈90% decrease in egg production	10	Reeve, et al. 1977
Copepods (adult), 5 genera	Mercuric chloride	10 days	≈70% decrease in faecal pellet production	10	Reeve, et al. 1977
Copepods (adult), 5 genera	Mercuric chloride	48 hrs	Hg-Cu interactions on LC50	17 (Hg in mixture)	Reeve, et al. 1977
Copepod (adult), *Acartia clausi*	Mercuric chloride	1.9 hrs	LC50	50	Corner & Sparrow, 1956

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Copepod (adult), *Pseudocalanus minutus*	Mercuric chloride	70 days	No growth of culture	5	Sonntag & Greve, 1977
Copepod (adult), *Pseudocalanus minutus*	Mercuric chloride	70 days	No growth inhibition	1	Sonntag & Greve, 1977
Barnacle (cyprid), *Balanus improvisus*	Mercuric chloride	48 hrs	About 50% abnormal development	16,600	Clarke, 1947
Barnacle (adult), *Balanus balanoides*	Mercuric chloride	48 hrs	LC90	1,000	Clarke, 1947
Barnacle (cyprid), *Balanus balanoides*	Mercuric chloride	6 hrs	About 10% reduciton in substrate attachment over 19 days	10	Pyefinch & Mott, 1948
Barnacle (cyprid), *Balanus balanoides*	Mercuric chloride	6 hrs	LC50	90	Pyefinch & Mott, 1948
Barnacles (nauplius), *Balanus crenatus*	Mercuric chloride	6 hrs	LC50	60	Pyefinch & Mott, 1948
Isopod (adult), *Jaera albifrons*	Mercuric chloride	5 days	Osmoregulation disruption in lowered salinity	100	Jones, 1975
Isopod (adult), *Jaera nordmanni*	Mercuric chloride	57 days	LC95	100	Jones, 1973
Isopod (adult), *Jaera albifrons sensu*	Mercuric chloride	<24 hrs	LC100	100	Jones, 1973
Isopod (adult), *Idotea neglecta*	Mercuric chloride	<24 hrs	LC100	100	Jones, 1973
Isopod (adult), *Idotea emarginata*	Mercuric chloride	<24 hrs	LC90	100	Jones, 1973
Grass shrimp (larva), *Palaemonetes vulgaris*	Mercuric chloride	<24 hrs	LC100	56	Shealy & Sandifer, 1975
Grass shrimp (larva), *Palaemonetes vulgaris*	Mercuric chloride	48 hrs	LC0	<5.6	Shealy & Sandifer, 1975

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Grass shrimp (larva), Palaemonetes vulgaris	Mercuric chloride	48 hrs	LC50	10	Shealy & Sandifer, 1975
Grass shrimp (larva), Palaemonetes vulgaris	Mercuric chloride	48 hrs	Abnormal development	10-18	Shealy & Sandifer, 1975
Crab (adult), Carcinus maenas	Mercuric chloride	48 hrs	LC50	1,000	Portmann, 1968
Crab (adult), Carcinus maenas	Mercuric chloride	48 hrs	LC50	1,200	Connor, 1972
Crab (larva), Carcinus maenas	Mercuric chloride	47 hrs	LC50	10	Connor, 1972
Crab (larva), Carcinus maenas	Mercuric chloride	20-30 hrs	LC50	33	Connor, 1972
Crab (larva), Carcinus maenas	Mercuric chloride	4.3-13.5 hrs	LC50	100	Connor, 1972
Crab (larva), Carcinus maenas	Mercuric chloride	2.7 hrs	LC50	1,000	Connor, 1972
Crab (larva), Carcinus maenas	Mercuric chloride	0.5 hrs	LC50	3,300	Connor, 1972
Crab (larva), Carcinus maenas	Mercuric chloride	0.22 hrs	LC50	10,000	Connor, 1972
White shrimp (adult), Penaeus setiferus	Mercuric chloride	60 days	No effect on respiration, growth, or molting	1	Green, et al. 1976
Hermit crab (adult), Pagurus longicarpus	Mercuric chloride	168 hrs	LC0	10	Eisler & Hennekey, 1977
Hermit crab (adult), Pagurus longicarpus	Mercuric chloride	168 hrs	LC50	50	Eisler & Hennekey, 1977
Hermit crab (adult), Pagurus longicarpus	Mercuric chloride	168 hrs	LC100	125	Eisler & Hennekey,

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Fiddler crab (adult), Uca pugilator	Mercuric chloride	28 days	Low survival, inhibited limb regeneration	1,000	Weis, 1976
Fiddler crab (adult), Uca pugilator	Mercuric chloride	6 days	20-25% reduction in percent survival	180	Vernberg & Vernberg, 1972
Fiddler crab (adult), Uca pugilator	Mercuric chloride	24 hrs	Increased oxygen consumption	180	Vernberg & Vernberg, 1972
Fiddler crab (zoea), Uca pugilator	Mercuric chloride	8 days	LC50	1.8	Decoursey & Vernberg, 1972
Fiddler crab (zoea), Uca pugilator	Mercuric chloride	24 hrs	20-100% increase in metabolic rate after stage I zoea	1.8	Decoursey & Vernberg, 1972
Fiddler crab (zoea), Uca pugilator	Mercuric chloride	5 days	About 40% increase in swimming activity of stage V zoea	1.8	Decoursey & Vernberg, 1972
Shiner perch, Cymatogaster aggregata	Mercuric chloride	-	45% reduction of brain cholinesterase activity	33,900	Abou-Donia & Menzel, 1967
Haddock (embryo), Melanogrammus aeglefinus	Mercuric chloride	96 hrs	LC50	918	U.S. EPA, 1980
Mummichog (adult), Fundulus heteroclitus	Mercuric chloride	168 hrs	LC0	100	Eisler & Hennekey, 1977
Mummichog (adult), Fundulus heteroclitus	Mercuric chloride	168 hrs	LC50	800	Eisler & Hennekey, 1977
Mummichog (adult), Fundulus heteroclitus	Mercuric chloride	168 hrs	LC100	1,000	Eisler & Hennekey, 1977
Mummichog (adult), Fundulus heteroclitis	Mercuric chloride	24 hrs	Disrupted osmoregulation	125	Renfro, et al. 1974
Mummichog (adult), Fundulus heteroclitus	Mercuric chloride	28 days	Up to 40% reduction in enzyme activity before recovery	12	Jackim, 1973

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Mummichog (embryo), *Fundulus heteroclitus*	Mercuric chloride	3 days	Many developmental abnormalities	30-40	Weis & Weis, 1977
Mummichog (embryo), *Fundulus heteroclitus*	Mercuric chloride	3 days	Some developmental abnormalities	10-20	Weis & Weis, 1977
Mummichog (embryo), *Fundulus heteroclitus*	Mercuric chloride	12 hrs	Some developmental abnormalities	30-40	Weis & Weis, 1977
Mummichog (adult), *Fundulus heteroclitus*	Mercuric chloride	-	Mercury redistribution organs following Se pretreatment	1,000 ug Hg/kg body wt plus 400 ug Se/kg body wt	Sheline & Schmidt Nielson, 1977
Mummichog (adult), *Fundulus heteroclitus*	Mercuric chloride	96 hrs	Cellular degeneration	250-5,000	Gardner, 1975
Mummichog (adult), *Fundulus heteroclitus*	Mercuric chloride	48 hrs	LC100	2,000	Eisler, et al. 1972
Mummichog (adult), *Fundulus heteroclitus*	Mercuric chloride	96 hrs	Sluggish uncoordinated swimming	1,150	Klaunig, et al. 1975
Winter flounder (adult), *Pseudopleuronectes americanus*	Mercuric chloride	60 days	Decreased respiration	10	Calabrese, et al. 1975
Striped bass (adult), *Morone saxatilis*	Mercuric chloride	30 days	Decreased respiration 30 days post exposure	5	Dawson, et al. 1977
Sea urchin (spermatazoa), *Arbacia punctulata*	Mercuric chloride	8 min	About 150% increase in swimming speed	20	Young & Nelson, 1974
Sea urchin (spermatazoa), *Arbacia punctulata*	Mercuric chloride	24 min	About 80% decrease in swimming speed	2,000	Young & Nelson, 1974
Starfish (adult), *Asterias forbesi*	Mercuric chloride	168 hrs	LC0	10	Eisler & Hennekey, 1977
Starfish (adult), *Asterias forbesi*	Mercuric chloride	168 hrs	LC50	20	Eisler & Hennekey, 1977

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Starfish (adult), *Asterias forbesi*	Mercuric chloride	168 hrs	LC100	125	Eisler & Hennekey, 1977
Sea urchin (embryo), *Arbacia punctulata*	Mercuric chloride	13 hrs	Abnormal development	92	Waterman, 1937
Echinoderm (larva), *Paracentrotus lividus*	Mercuric chloride	40 hrs	Retarded growth & development	3	Soyer, 1963
Protozoan, *Cristigera* spp.	Mercuric chloride	12 hrs	Reduced growth	2.5-5	Gray & Ventilla, 1973
Protozoan, *Euplotes vannus*	Mercuric chloride	48 hrs	Inhibition reproduction	1,000	Persoone & Uyttersprot, 1975
			Methylmercuric Compounds		
Alga, *Dunaliella tertiolecta*	Methylmercuric chloride	10 min	EC50 photosynthesis	about 170	Overnell, 1975
Alga, *Phaeodactylum tricornutum*	Methylmercuric chloride	25 days	EC50 photosynthesis	about 190	Overnell, 1975
Red alga (sporling), *Plumaria elegans*	Methylmercuric chloride	18 hrs	LC50 after 7 days	44	Boney, et al. 1959
Mummichog (adult), *Fundulus heteroclitus*	Methylmercuric chloride	24 hrs	Disrupted osmoregulation	125	Renfro, et al. 1974
Oyster (adult), *Crassostrea virginica*	Methylmercuric chloride	19 days	Trace metal upset	50	Kopfler, 1974
Amphipod (adult), *Gammarus duebeni*	Methylmercuric chloride	3 days	Induced diuresis	56	Lockwood & Inman, 1975
Fiddler crab (adult), *Uca* spp.	Methylmercuric chloride	32 days	No limb regeneration	300-500	Weis, 1977
Fiddler crab (adult), *Uca* spp.	Methylmercuric chloride	32 days	Melanin absent in regenerated limbs	100	Weis, 1977
Blue mussel (adult), *Mytilus edulis*	Methylmercuric chloride	24 hrs	About 90% reduced feeding rate	400	Dorn, 1976

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Diatom, Nitzchia delicatissima	Methylmercuric dicyandiamide	24 hrs	EC50 photosynthesis	0.4	Harriss, et al. 1970
Alga, Chaetoceros sp.	Dimethylmercury	3 days	About 75% reduction in growth	100	Hannan & Patouillet, 1972
Alga, Cyclotella sp.	Dimethylmercury	3 days	About 15% reduction in growth	500	Hannan & Patouillet, 1972
Alga, Phaeodactylum sp.	Dimethylmercury	3 days	About 45% reduction in growth	500	Hannan & Patouillet, 1972
Red alga (sporling), Plumaria elegans	Methylmercuric chloride	25 min	EC50 growth over 21 days	40	Boney, 1971
			Other Mercury Compounds		
Dinoflagellate, Gymnodinium spe[illegible]ns	Mercuric acetate	11 days	55% reduction in growth	10	Kayser, 1976
Dinoflagellate, Gymnodinium spendens	Mercuric acetate	4 days	No growth of culture	100	Kayser, 1976
Dinoflagellate, Scrippsiella faeroense	Mercuric acetate	25 days	45% reduction in growth, morphological variation	10	Kayser, 1976
Dinoflagellate, Scrippsiella faeroense	Mercuric acetate	14 days	No growth of culture	1,000	Kayser, 1976
Oyster (adult), Crassostrea virginica	Mercuric acetate	15 days 12 hrs daily	33% reduction in shell growth	10	Cunningham, 1976
Oyster (adult), Crassostrea virginica	Mercuric acetate	60 days	LC55	100	Cunningham, 1976
Copepod (adult), Acartia clausi	Mercuric acetate	1.9 hrs	LC50	50	Corner & Sparrow, 1956
Red alga (sporling), Plumaria elegans	Mercuric iodide	18 hrs	LC50 after 7 days	156	Boney, et al. 1959

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Diatom, *Nitzchia delicatissima*	N Methylmercuric-1,2,3,6-tetrahydro-3,6-methano-3,4,5,6,7,7-hexachlorophthalimine	24 hrs	EC50 photosynthesis	0.3	Harriss, et al. 1970
Red alga (sporling), *Plumaria elegans*	Ethylmercuric chloride	18 hrs	LC50 after 7 days	26	Boney, et al. 1959
Copepods (adult), *Acartia clausi*	Ethylmercuric chloride	1.9 hrs	LC50	50	Corner & Sparrow, 1956
Alga, *Chlorella* sp.	Ethylmercuric phosphate	10 days	22% reduction in growth	0.6	Ukeles, 1962
Alga, *Chlorella* sp.	Ethylmercuric phosphate	10 days	100% lethal to culture	6	Ukeles, 1962
Alga, *Dunaliella euchlora*	Ethylmercuric phosphate	10 days	36% reduction in growth	0.6	Ukeles, 1962
Alga, *Dunaliella euchlora*	Ethylmercuric phosphate	10 days	100% lethal to culture	60	Ukeles, 1962
Alga, *Monochrysis lutheri*	Ethylmercuric phosphate	10 days	No reduction in growth	0.6	Ukeles, 1962
Alga, *Monochrysis lutheri*	Ethylmercuric phosphate	10 days	100% lethal to culture	6	Ukeles, 1962
Alga, *Phaeodactylum tricornutum*	Ethylmercuric phosphate	10 days	45% reduction in growth	0.6	Ukeles, 1962
Alga, *Phaeodactylum tricornutum*	Ethylmercuric phosphate	10 days	100% lethal to culture	6	Ukeles, 1962
Alga, *Protococcus* sp.	Ethylmercuric phosphate	10 days	14% reduction in growth	0.6	Ukeles, 1962
Alga, *Protococcus* sp.	Ethylmercuric phosphate	10 days	100% lethal to culture	6	Ukeles, 1962

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Red alga (sporling), *Plumaria elegans*	Phenylmercuric chloride	18 hrs	LC50 after 7 days	54	Boney, et al. 1959
Oyster (adult), *Crassostrea virginica*	Phenylmercuric chloride	19 days	Trace metal upset	50	Kopfler, 1974
Diatom, *Nitzchia delicatissima*	Phenylmercuric acetate	24 hrs	EC50 photosynthesis	1.5	Harriss, et al. 1970
Stickleback (adult), *Gasterosteus aculeatus*	Phenylmercuric acetate	370 min	LC100	100	Boetius, 1960
Red alga (sporling), *Plumaria elegans*	Phenylmercuric iodide	18 hrs	LC50 after 7 days	104	Boney, et al. 1959
Diatom, *Nitzchia delicatissima*	Diphenylmercury	24 hrs	EC50 photosynthesis	18	Harriss, et al. 1970
Sockeye salmon (juvenile), *Oncorhynchus nerka*	Pyridylmercuric acetate	12-15 wks, 1 hr wkly	1.2 mg Hg/kg wet wt muscle 12 weeks post-exposure	1,000	Amend, 1970
Sockeye salmon (adult), *Oncorhynchus nerka*	Pyridylmercuric acetate	12-15 wks, hr wkly as juveniles	0.24 mg Hg/kg wet wt muscle 3 yrs post-exposure	1,000	Amend, 1970
Sockeye salmon (adult), *Oncorhynchus nerka*	Pyridylmercuric acetate	12 1-hr exposures as juveniles	0.04 mg Hg/kg wet wt muscle 4 yrs post-exposure	1,000	Amend, 1970
Silver salmon (adult), *Oncorhynchus kisutch*	Pyridylmercuric acetate	12-15 wks as juveniles 1 hr wkly	0.03 mg Hg/kg wet wt muscle 2 yrs post-exposure	1,000	Amend, 1970
Chinook salmon (adult), *Oncorhynchus tshawytscha*	Pyridylmercuric acetate	35 wks as juveniles 1 hr wkly	up to 0.12 mg Hg/kg muscle 4 yrs later	1,000	Amend, 1970
Red alga (sporling), *Plumaria elegans*	Isoamylmercuric chloride	18 hrs	LC50 after 7 days	19	Boney, et al. 1959

Table 6. (Continued)

Species	Chemical	Duration	Effect	Result* (µg/l)	Reference
Red alga (sporling), *Plumaria elegans*	N-Amylmercuric chloride	18 hrs	LC50 after 7 days	13	Boney, et al. 1959
Red alga (sporling), *Plumaria elegans*	Isopropylmercuric chloride	18 hrs	LC50 after 7 days	28	Boney, et al. 1959
Red alga (sporling), *Plumaria elegans*	N-Propylmercuric chloride	18 hrs	LC50 after 7 days	13	Boney, et al. 1959
Red alga (sporling), *Plumaria elegans*	N-Butylmercuric chloride	18 hrs	LC50 after 7 days	13	Boney, et al. 1959

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* Results are expressed as mercury, not as the compound.

** Static, continual loss over time.

*** Not at steady-state.

****BCF independent of concentration in water over range tested.

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Mammalian Toxicology and Human Health Effects

Human beings are exposed to a variety of physical and chemical forms of mercury. Since these forms differ in their toxicity and in the hazard they present to human health it will be necessary in many parts of this document to treat these forms separately from the point of view of hazard evaluation. The situation is made even more complicated by our lack of knowledge of the forms of mercury in water. Thus, the approach being taken is to discuss the most important forms of mercury to which humans are exposed, and from this to evaluate the importance of intake from the water supply.

At this point, it is useful to give at least general definitions of the usual forms that mercury can take. It is customary (Maximum Allowable Concentrations Committee, 1969) to consider three broad categories of the physical and chemical forms of mercury. These categories are selected mainly because of the difference in their toxic properties and in the hazards they present to human health. The first category consists of metallic mercury. Mercury in the zero oxidation state (Hg^0) is usually referred to as mercury vapor when present in the atmosphere or as metallic mercury when present in its liquid form. The second category comprises the inorganic compounds of mercury, which include the salts of the two oxidation states of mercury, Hg_2^{++} (mercurous salts), and Hg^{++} (mercuric salts). The third major category contains the so-called organic mercurials or organic mercury compounds. These are defined as those compounds of mercury in which mercury is attached to at least one carbon atom by a covalent bond. The toxic properties in this third category, however, vary enormously. The most important subgroup in the organo-mercurials category is comprised of the methylmercury and related short-chain alkyl mercurial compounds. From the point of view of environmental exposures, the methylmercury compounds are the ones of greatest concern. The other organo-mercurials may take the form of aryl and alkoxy-aryl mercurials as well as a wide variety of other organo-mercurials used in medicine and agriculture. In general these organic forms of mercury are much less toxic than the short-chain alkyl mercurials.

The main sources of human mercury exposure are methylmercury compounds in the food supply and mercury vapor in the atmosphere of occupational settings. Exposure to other forms of mercury result from occupational, medicinal, or accidental circumstances. As will be discussed later, the water supply probably contains mercury mainly in the form of Hg^{++} salts complexed with a variety of constituents in water.

The topics of mercury in the environment, human exposure to mercury, and an estimate of health effects and hazards of mercury have been the subject of many reviews by expert committees and individual authors over the past ten years. Included are reviews by the Swedish Expert Group (1971); Norton (1971); World Health Organization (WHO, 1971, 1972, 1976); Miller and Clarkson (1973); Friberg and Vostal (1972); Nordberg (1976); and The National Academy of Sciences (NAS, 1978). Additional references are Hartung and Dinman (1972), and Buhler (1973).

The source material for this document comes primarily from original scientific publications, but the reviews mentioned above have also been of inestimable value in the preparation of this document and in developing an overall perspective of the mercury problem. Special mention should be made of the review prepared by the WHO (1973) where the recommended safe levels of mercury in water are discussed.

INTRODUCTION

A variety of original articles and reviews have dealt with sources, pathways and mechanisms of transport, and sinks of mercury in the environment. These include Wallace, et al. (1971); D'Itri (1972); Friberg and Vostal (1972); Garrels, et al. (1973); Kothny (1973); WHO (1972, 1976); Heindryckx, et al. (1974); Korringa and Hagel (1974); Wollast, et al. (1975); Abramovskig, et al. (1975); and National Academy of Sciences (NAS, 1978). In view of the number of recent reviews, and the fact that a review has just been completed by a National Academy of Sciences panel, no attempt will be made in this section to deal with this subject in detail except to emphasize those data that deal directly with human uptake of mercury from the water supply.

The dynamics of mercury in the environment may be viewed in the context of a global cycle. This cycle presents a general perspective within which man's contribution to the environmental mercury burden may be viewed. However, before quoting numbers related to the global turnover of this element, several caveats are in order. Many of the calculations involve assumptions for which supporting experimental evidence is tenuous, to say the least. Concentrations of mercury in certain environmental samples (e.g., in fresh water and ocean water) are so low as to challenge the skill of the best analyst using the most sophisticated modern equipment. Matsunaga, et al. (1979) have recently reviewed the methodological errors involved in the measurement of mercury in seawater. These analytical figures are multiplied by huge numbers, e.g., the area of oceans (361×10^{12} m^2) and the precipitation over oceans ($4.11 \times 10^{17} l/m^2$ yr), to calculate the "mercury budgets" for the global cycle. Authorities differ in their interpretation of certain environmental samples and the most recent data seem to conflict with earlier data (NAS, 1978; Korringa and Hagel, 1974). It is likely, therefore, that the "up-dating" of the global cycle and other more localized cycles will continue. Nevertheless, certain general conclusions have survived the test of time and are useful in developing a perspective with regard to human exposure to mercury and the possibilities of control.

The Global Cycle of Mercury: The atmosphere is the major pathway for distribution of mercury. Most reviewers are in good agreement that the total entry into the atmosphere ranges from 40,000 to 50,000 tons* per year (Table 1) on a worldwide basis. The main input to the atmosphere is from natural sources. Emission (degassing) from continental land masses accounts for about 66 percent of the total natural input. Emission from the ocean surface is next in importance, whereas emission from land biota and volcanoes seems to be negligible.

Manmade (anthropogenic) release, although less than that due to natural causes, is substantial, accounting for about one-third of total input.

The amount of mercury contained in the atmosphere is the subject of widely divergent figures (Table 2). The main point of contention is the assumption with regard to the change of atmospheric mercury concentration with height. The most recent review of the subject (NAS, 1978) assumed an exponential decline with increasing altitude, whereas others have assumed mercury mixes to a height of 1 kilometer (Heindryckx, et al. 1974). A Japanese group has calculated the residence time of Hg in the atmosphere to be 5.7 years (Katsuniko and Takumi, 1976).

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*"Tons" are metric tons, i.e., 1,000 kg, in this text.

TABLE 1

Entry of Mercury into the Atmosphere

Source	Annual input (metric tons) (1)	(2)	(3)
Natural			
Continental degassing	17,800		50,000
Oceanic emission	7,600		
Coastal emission	1,420		
Emission from land biota	40		
Volcanic	20		
Total	26,880	25,000	
Anthropogenic	10,000	16,000	
Total	36,880	41,000	

(1) National Academy of Sciences, 1978
(2) Korringa and Hagel, 1974
(3) Heindryckx, et al. 1974

TABLE 2

The Amount of Mercury in some Global Reservoirs

Reservoir	Mercury Content (metric tons) (1)	(2)
Reservoir		
Atmosphere	850	
Freshwater	2000	
Freshwater biota[a]	400	
Oceanwater	41×10^6	70×10^6
Oceanic Biota[b]	200,000	

(1) National Academy of Sciences, 1978
(2) WHO, 1976
[a] Only living biota
[b] Living and dead biota

Mercury is removed from the atmosphere mainly by precipitation. The National Academy of Sciences (1978) has calculated that about 280 metric tons/year of mercury are deposited into fresh water from the atmosphere. Although this is less than other sources of input (730 metric tons/year), variations in distribution of atmospheric deposition might lead to substantial local pollution.

Most of the atmospheric transport goes to the oceans (Table 3). Figures vary widely. The most recent estimates indicate deposition from the atmosphere to be about 11,000 metric tons/year. The entry of mercury into the ocean from all known sources seems not to exceed about 50,000 metric tons/year although the contribution from hydrothermal sources is unknown and may be important (U.K. Dep. Environ., 1976).

The amount of mercury contained in the oceans is extremely large compared to the known inputs. Most estimates (see Table 2) fall in the range of 41 million to 70 million tons. Based on the figures given in Tables 2 and 3, it is clear that mercury concentrations in the open oceans (as opposed to coastal and inland waters) have not changed significantly. Oceanic fish levels most probably have remained unchanged by man's activities, especially in wide ranging oceanic fish such as shark, swordfish, and tuna.

Mercury in living biota accounts for about one-half of the total mercury in freshwater. The figures in Table 2 are expressed in terms of total mercury. If expressed in terms of methylmercury, the amount of mercury in biota would considerably exceed that in freshwater.

Data on concentrations of mercury in the lithosphere have been reviewed by several expert groups (World Health Organization WHO, 1976; U.K. Dep. Environ., 1976; NAS, 1978). Mercury concentrations in nonmineralized soils vary over two orders of magnitude, the average concentration being about

TABLE 3

Entry of Mercury into the Ocean

Source	Annual input (metric tons)		
	(1)	(2)	(3)
Atmospheric deposition		41,000	50,000
Open Ocean and Polar	7,600		
Coastal waters	3,600	5,000	5,000
Land runoff			
Soluble	1,600		
Particulate	3,700	5,000	5,000
Hydrothermal	*	*	*

(1) National Academy of Sciences, 1978
(2) Korringa and Hagel, 1974
(3) Heindryckx, et al. 1974

*No data available

0.07 µg Hg/g. Freshwater sediments in nonpolluted rivers and lakes in the United States usually contain less than 0.1 µg/g (wet sediment). Insufficient data exist to calculate average values and ranges of mercury concentrations in oceanic sediments.

Mercury is strongly bound to soil and is predominantly attached to organic matter (Anderson, 1976; Keckes and Miettinen, 1970; Landry, et al. 1978). Kimura and Miller (1970) reported that mercury mobility is minimal even in soils contaminated by mercury fungicides. However, Fuller (1978) has reported that the mobility of mercury in soils is increased in the presence of leachates from municipal landfills.

Chemical and Physical Forms of Mercury in the Environment and Their Transformation: Mercury occurs in a variety of physical and chemical forms in nature. Mercury is mined as cinnabar (HgS) but in some areas (Almaden, Spain) the ore is so rich that metallic mercury is also present.

Human activities have resulted in the release of a wide variety of both inorganic and organic forms of mercury (Table 4). The electrical and chloralkali industries and the burning of fossil fuels release mercury to the atmosphere mainly as Hg^{0}. Release to water via direct discharge involves Hg^{++} and Hg^{0} (e.g., chloralkali). Methylmercury compounds have been released to fresh and oceanic water in Japan as a byproduct of the manufacture of aceteldehyde and vinyl chloride. Other anthropogenic sources have resulted in release of aryl and alkoxy-aryl compounds as well as methyl- and ethylmercury compounds used as fungicides.

The inorganic forms of mercury may undergo oxidation-reduction reactions in water as indicated by the equations:

TABLE 4

Patterns of Mercury Consumption in the United States*

End use	Annual Consumption (percent total)		
	1970	1973	1975[1]
Electric Apparatus	26	33	32
Caustic Chloride (chloralkali)	25	24	23
Paints	17	14	5.1
Industrial Instruments	7.9	13	21
Dental	3.7	4.9	6.2
Catalysts	3.7	1.2	0.8
Agriculture	3.0	3.4	1.1
Laboratories	3.0	1.2	?
Pharmaceuticals	1.1	1.1	0.8
Others	9.6	4.2	9.8
Total consumption (metric tons)	2100	1867	2091

*Source: NAS, 1978; U.S. EPA, 1975a

[1] The percentages were estimated under the assumption that consumption by laboratories was negligible.

$$2\ Hg^0 = Hg_2^{++} + 2\ e^- \ldots\ldots (1)$$

$$Hg_2^{++} = 2Hg^{++} + 2\ e^- \ldots\ldots (2)$$

Stock and Cucuel (1934) have demonstrated that Hg^0 can be oxidized to Hg^{++} in water in the presence of oxygen. The reaction probably takes place in rain droplets during removal of Hg^0 from the atmosphere by precipitation. Wallace, et al. (1971) have noted that mercury concentrations as high as 40 g/l can be attained when water saturated with oxygen is exposed to mercury vapor. The mercurous form of mercury (Hg_2^{++}) undergoes disproportionation to Hg^0 and Hg^{++} in the presence of sulfur ligands (Cotton and Wilkinson, 1966). Jensen and Jernelov (1972) have noted that the presence of organic substances in water facilitates the transformation of Hg^0 to Hg^{++}. The mercuric ion, Hg^{++}, is the substrate for the biomethylation reaction that occurs in microorganisms present in aquatic sediments (Figure 1).

In a recent review by the National Academy of Sciences (1978), it was noted that the main pathway of methylation of soluble Hg^{++} involved a transfer of methyl groups from methyl cobalamine (methyl-B_{12}) and that the rate of formation of methylmercury is largely determined by the concentrations of soluble Hg^{++} and methyl B_{12}.

Both dimethyl mercury and monomethyl mercury may be formed by bacteria present in sediments. The formation of dimethyl mercury is favored by a high pH. Dimethyl mercury is volatile and may enter the atmosphere, where it may undergo decomposition to yield Hg^0 (Wood, 1976). It may also be converted to monomethyl mercury in rainfall especially in acid rains containing Hg^{++}. In the presence of Hg^{++}, one molecule of dimethyl mercury is converted to two molecules of monomethyl mercury (Cotton and Wilkinson, 1966).

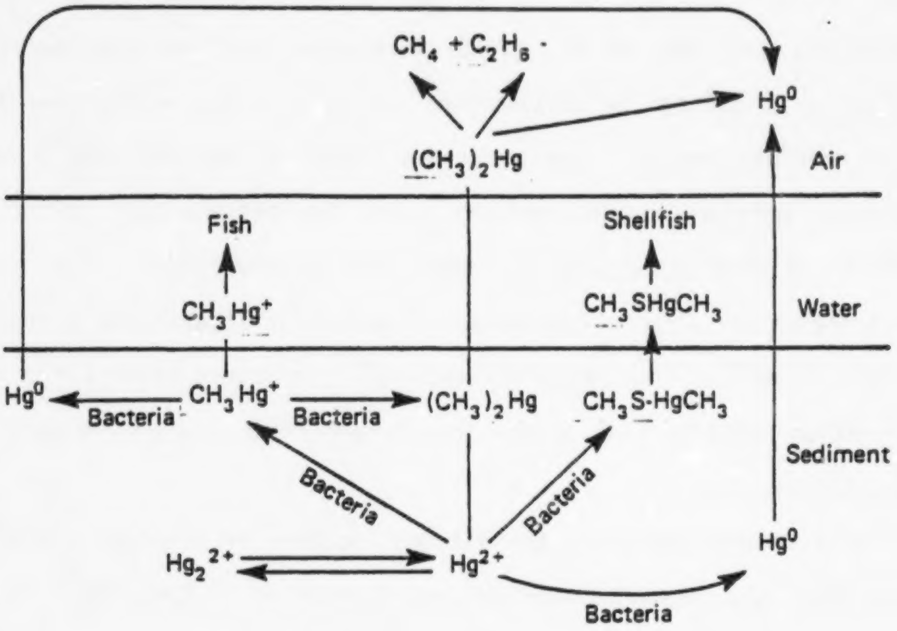
$CH_4 + C_2H_6$
Hg^0
$(CH_3)_2Hg$
Air
Fish
Shellfish
CH_3Hg^+
CH_3SHgCH_3
Water
Hg^0
Bacteria
CH_3Hg^+
Bacteria
$(CH_3)_2Hg$
$CH_3S\text{-}HgCH_3$
Sediment
Bacteria
Bacteria
Hg^0
Hg_2^{2+}
Hg^{2+}
Bacteria

Figure 1.

The mercury cycle demonstrating the bioaccumulation of mercury in fish and shellfish.

Source: NAS, 1978

A variety of bacterial and fungal organisms have the capacity to methylate Hg^{++}. Jensen and Jernelov (1972) have pointed out that conditions which promote bacterial growth will enhance methylation of mercury. Thus, the highest rates of methylation in the aquatic environment are seen in the uppermost part of the organic sediments and in suspended organic material in water. Furthermore, those microorganisms able to methylate mercury at high rates are also usually resistant to the toxic effect of Hg^{++}.

Microorganisms are also capable of demethylating methylmercury compounds and of splitting the carbon-mercury bond in a variety of other organic mercurials. This process involves: first, the cleavage of the carbon-mercury bond to release Hg^{++} and, second, the reduction of Hg^{++} to Hg^{0}. Both processes are enzyme-mediated (NAS, 1978). Microorganisms capable of demethylation reactions have been shown to occur in aquatic sediments, soils, and human fecal material. Microbial resistance to methylmercury correlates with the capacity to convert methylmercury to Hg^{0}. Both methylation and demethylation rates have been measured in aquatic sediments in the laboratory (for review, see NAS, 1978). In general, methylation and demethylation account for the conversion of a small fraction of the total mercury in the sediment on an annual basis (probably 5 percent or less). The total production of methylmercury in freshwater on a global scale was estimated to be about 10 metric tons per year and in the oceans to be about 480 metric tons/year.

Divalent inorganic mercury (Hg^{++}) may undergo reduction to Hg^{0}. Certain widely occurring bacteria such as Pseudomonas have been shown to be capable of this reduction (Magos, et al. 1964; Furukawa, et al. 1969). Yeast cells also carry out this reaction and the capacity to do this correlates with a resistance to the toxic effects of Hg^{++} (Singh and Sherman, 1974).

In addition to being a substrate for both methylation and reduction reactions in microorganisms, Hg^{++} is available to form a variety of precipitates, complexes, and chelates in water. A stable precipitate is formed with the sulfide ion, $S^{=}$. The latter is usually present in anaerobic aquatic environments. The formation of HgS may limit the amount of mercury available for methylation reactions (Jensen and Jernelov 1972). However, our knowledge of the chemical forms of mercury in natural waters is incomplete. For theoretical reasons, the degree of oxygenation, pH, and the presence of inorganics (e.g., Cl^-), and organics (e.g., $-S^-$, COO^-, and N in organic matter in water), ligands are probably important factors in determining the chemical species of mercury in water. On thermodynamic grounds, one would expect inorganic mercury to be present mainly as Hg^{++} compounds in well oxygenated water and an increasing fraction of mercury as Hg^0 or HgS in reducing conditions (NAS, 1978). In view of the high concentrations of chloride and, to a lesser extent, bromide anions in sea water, inorganic mercury should be present as various halide complexes ($HgCl_4^{=}$, $HgCl_3B^{=}$, $HgCl_3^-$, $HgCl_2Br^-$, $HgCl_2$) in marine water.

Methylmercury compounds readily pass across cell membranes and bind to tissue ligands. Thus, methylmercury tends to be removed from water by living biota. Fagerstrom and Asell (1973) have concluded that the concentration of methylmercury in water is of major importance for the end result in terms of fish accumulation. This conclusion was based on a mathematical model of methylmercury accumulation in a simple food chain.

Limited information is available on concentrations of methylmercury in fresh or marine water (see Table 5). Chau and Saitoh (1973) were unable to detect methylmercury (detection limit 0.24 ng Hg/l) in unfiltered Great Lakes water, and measured 0.5 to 0.7 ng Hg/l in four small mercury-polluted

TABLE 5

A Survey of Reported Methylmercury Concentrations in Natural Waters*

Location	CH_3Hg Detection Limit ng/l	CH_3Hg Conc (ppt) Mean/Range ng/l	Total Hg Conc (ppt) Mean/Range ng/l	$\frac{CH_3Hg}{\text{Total Hg}}$ %	References
Canada					
Most Lakes and Rivers	<0.25	<0.25	–	–	Chow and Saitoh (1973)
Lake St. Clair) Clay Lake) Pinchi Lake)		0.5–1.7	–	–	Chou and Saitoh (1973)
Sweden					
Uncontaminated Lakes	0.1	0.1	<10	<1	Jernelov et al. (1975)
U.S.A.					
Mississippi River	1.0	1	30–40	1–3	Andren and Harris (1975)
N.W. Quebec					
Rivers	<0.5	<0.5	<0.5	5–50	McLean, et al. (1980)

*Source: McLean, et al. 1980.

lakes. Andren and Harris (1975) could not detect methylmercury in samples of river and coastal waters of the eastern Gulf of Mexico and McLean, et al. (1980) could not detect methylmercury in rivers in northwestern Quebec containing 5 to 50 ng/l of total mercury. In all the studies reported in Table 5, methylmercury accounted for less than 10 percent of the total mercury content of ambient water.

Wood (1976) has pointed out that, as a result of methylation and demethylation reactions, the concentrations of methylmercury will approach a steady state in any given ecosystem. The steady state concentration will be affected by any environmental factors that influence either or both reactions. Many factors may be involved, some of which have been mentioned above. However, there is a need for further studies on the dynamics of methylmercury in the environment.

EXPOSURE

Ingestion from Water

The concentrations of mercury in rainwater were reported by Stock and Cucuel (1934) to average 200 ng Hg/l, and to range from 50 to 480 ng Hg/l in Germany. Nearly 40 years later, Pierson, et al. (1973) reported that rainwater samples in the U.K. usually contained below 200 ng Hg/l. In Sweden, Eriksson (1967) found values of up to 200 ng Hg/l and Brune (1969) noted values of approximately 300 ng Hg/l in rainwater. Values of mercury concentrations in snow show considerable variability and probably depend greatly upon collection conditions and upon how long the snow has lain on the ground. Straby (1968) noted values of 80 ng Hg/kg in fresh snow but 400 to 500 ng Hg/kg in snow that may have partly melted or evaporated over the winter. Analyses of the Greenland ice sheet by Weiss, et al. (1971) and Weiss (1975) indicate values in the range of 13 to 230 ng Hg/l with no definite trends according to the age of the ice sample.

The WHO expert group (WHO, 1976) concluded that levels in noncontaminated freshwater were less than 200 ng Hg/l. Stock and Cucuel (1934) reported values in the range of 10 to 50 ng Hg/l of drinking water in Germany. The CEC International Symposium reviewed data on over 700 samples collected from drinking water and found that out of a total of 193 samples where Hg was found, 153 had values below 0.25 µg/l. No value above 0.8 µg/l was detected. The U.S. EPA (1975b) established that only 2.5 percent of 512 drinking water samples had mercury levels which exceeded the proposed 1975 Federal standard for drinking water of 2,000 ng Hg/l. A geological survey of mercury in U.S. rivers and estuaries reported by Wershaw (1970) found that more than half of the 73 rivers that were sampled had mercury concentrations lower than 1,000 ng Hg/lg and 34 of the rivers had concentrations of less than 100 ng Hg/l. Windom in 1973, reporting on measurements of the Savannah estuary found that concentrations ranged up to 450 ng Hg/l.

Fitzgerald (1979) has summarized data on mercury concentrations in estuarine waters. Values are reported in the range 2 to 450 ng/l. However, these values refer to total mercury, i.e. both dissolved and that found on suspended solids.

Reported mercury concentration in coastal waters also refer to both dissolved and particulate mercury (Fitzgerald, 1979). The mean values from 8 different studies did not exceed 62 ng/l. The median value was 17 ng/l.

Levels of mercury in ocean waters are usually below 300 ng Hg/l. Stock and Cucuel in 1934 reported a mean value of 30 ng Hg/l. Hosohara (1961) recorded mercury levels at different depths in the Pacific; values on the surface were about 80 to 150 ng Hg/l, and values at a depth of 300 meters were found to range between 150 and 270 ng Hg/l. Further details on the ocean mercury levels have been given in the publication by the U.K. Department of the Environment (1976). A recent review by Fitzgerald (1979) indicates that 95 percent of reported mean values are below 126 ng/l with a median value of about 15 ng/l. Matsunaga, et al. (1979), in the most recent report on mercury in waters, claim that 5 to 6 ng Hg/l "may be a reliable value for baseline of mercury in unpolluted oceans," which is roughly 10 to 100 times lower than concentrations reported above. The authors (Matsunaga, et al. 1979) attribute the wide scatter in previously reported values to problems in analytical techniques, i.e., contamination.

Most samples of drinking water obtained in the United States and Europe have mercury levels below 50 ng Hg/l. Assuming a daily consumption of 2 liters of water by the 70 kg standard man, this would correspond to a daily intake of 100 ng Hg. Values up to 200 ng Hg/l have been reported in water in areas with minerals rich in mercury. This concentration would indicate an intake of 400 ng Hg/day. Most mercury in fresh water is probably in the form of complexes of Hg^{++}. Gastrointestinal absorption of this form of mercury is less than 15 percent. Thus, an intake of 400 ng Hg/day would correspond to a retained dose of less than 100 ng Hg/day. The current drinking water standard in the United States is 200 ng Hg/l. This corresponds to a daily intake of 400 ng Hg or an estimated retained dose of 60 ng Hg.

Ingestion from Foods

The U.K. Department of the Environment (1976) and the National Academy of Sciences (1978) have reviewed the results of a large number of surveys of mercury concentrations in food. These surveys uniformly indicate that a distinction must be made between fish and nonfish food. In foodstuffs other than fish and fish products, the concentrations of mercury are so low as to be near or below the limit of detection of mercury by the analytical methods used in reported studies. In the United States, figures from surveys carried out by the Food and Drug Administration indicate that most foodstuffs have total mercury levels below 20 ng Hg/g. Meat and poultry may contain levels up to 200 ng Hg/g (NAS, 1978). In view of the uncertainties in these numbers, it is impossible to calculate average daily intakes for nonfish food in the United States. A low intake of mercury from nonfish sources is consistent with the finding that nonfish eaters have the lowest blood concentration of mercury.

A variety of surveys have been carried out in the United States of concentrations of mercury and the forms of mercury in fish (NAS, 1978). These surveys indicate that the average concentration of mercury in most fish is less than 200 ng/g, with virtually all the mercury in fish muscle in the form of methylmercury compounds. However, certain large carnivorous oceanic fish can regularly develop much higher levels. In general, over 50 percent of swordfish tested had values more than 1,000 ng/g. Observations on 3,000 samples of canned tuna indicated an average total mercury concentration of approximately 250 ng/g, with 4 percent of the samples being above 500 ng/g. Concentrations much higher than these, ranging to over 20,000 ng/g, have been reported in freshwater fish caught in heavily polluted areas (Fimreite and Reynolds, 1973). The oceanic fish in Minamata Bay in Japan also had values of this order of magnitude.

The age or length or weight of the fish appears to be an important factor in determining the mercury concentration in fish muscle for both freshwater and marine fish; the older the fish, the higher the mercury concentration. This is consistent with the report that the halftime of methylmercury in fish is of the order of 1,000 days (Miettinen, et al. 1969; Miettinen, 1972). Thus, accumulation might be expected to occur throughout the life of these species. In general, fish that are carnivorous and are at the end of a food chain tend to have the highest concentrations. Thus, freshwater fish such as the northern pike and oceanic fish such as the shark and swordfish have elevated mercury levels compared to other fish. Marine mammals can also accumulate mercury. For example, the livers of seal may attain very high concentrations of total mercury in the order of 340,000 ng/g, but over 90 percent of this is in the form of inorganic mercury probably combined in an inert form with selenium (Koeman, et al. 1973). Nevertheless, sufficient amounts of methylmercury are found in seal tissue, including liver, so that individuals consuming seal meat, such as Eskimos, may develop high blood concentrations of methylmercury (Galster, 1976).

Observations on museum specimens of tuna fish and swordfish suggest that the concentrations of mercury have not changed throughout this century. For example, Miller, et al. (1972) found mercury concentrations in tuna ranging from 180 to 640 ng/g, which may be compared with present values in tuna ranging roughly from 200 to 1,000 ng/g wet weight. The lack of observable change in mercury levels in tuna and other oceanic fish is consistent with the large reservoir of mercury in the oceans.

The U.S. Department of Commerce (1978) has published data relating to the intake of mercury from fish in the diet of the U.S. population. Mercury analyses were made on the edible tissues of 19,000 samples of fish representing all major recreational species of the U.S. collected in 1971-73. Information on seafood consumption was obtained from a survey of 25,647 panelists who maintained a diary of their fish consumption. One-twelfth of the panelists recorded consumption each month for 1 year from September, 1973 to August 1974. The selected data from these studies are given in

Table 6. Approximately 95 percent of the panelists reported eating fish. Tuna fish was by far the most popular item with 68 percent of the fish eaters reporting they ate tuna fish. Since 20 percent did not report the species of fish consumed, and assuming that a high proportion of this group in fact consumed tuna, the proportion eating tuna would be about three-quarters of the test population. By comparison, the next most popular species of fish was flounder, eaten by only 13 percent.

The average concentration of mercury in tuna is one of the highest in the group of fish species consumed by more than 5 percent of the panelists. It is clear, therefore, that the consumption of tuna fish in the United States accounts for most of the dietary intake of methylmercury, as this form of mercury accounts for more than 90 percent of the total mercury in tuna and most other species of fish.

The data in Table 6 do not allow an estimate of the average daily intake. However, if we assume (a) FDA figure of 27 g fish/day as the upper 95 percent of fish intake in the U.S. population; (b) an average value of 220 ng Hg/g for mercury in tuna; and (c) that 75 percent of the fish consumption is tuna, it follows that 95 percent of the population consumes less than 4,500 ng Hg/day as methylmercury from tuna. Contributions from other fish listed in Table 5 would be less than 1,000 ng Hg/day assuming an average concentration of 100 ng Hg/g fish. Thus, it seems likely that 95 percent of the population will consume less than 5,000 ng Hg as methylmercury per day from fish. If the average daily fish consumption in the United States is taken as 18.7 g instead of 27 g (Cordle, et al. 1978), the average methylmercury consumption from fish would be 3,000 ng Hg/day/70 kg person.

The U.S. Department of Commerce Report (1978) did not give estimates of daily intakes of mercury from fish. The report did, however, calculate the

TABLE 6

Average and Maximum Mercury Levels in Species of Fish Eaten by 2 Percent or More of 24,652 Panelists*

Species[a]	Panelists (percent)	Mercury concentration[b] µg Hg/g fresh weight Average	Maximum	Number[c] of Fish in sample
Tuna (light)	68	0.14 (skipjack)	0.39	70
		0.27 (yellow fin)	0.87	115
Shrimp	21	0.05	0.33	353
Flounder	13	0.10	0.88	1179
Perch (marine)	10	0.13	0.59	268
Salmon	10	0.05	0.21	806
Clams	9	0.05	0.26	584
Cod	6	0.13	0.59	134
Pollock	5.9	0.14	0.95	227
Haddock	5.8	0.11	0.37	88
Herring	5.1	0.02	0.26	272
Oysters	5.0	0.03	0.45	260

*Source: U.S. Dept of Commerce, 1978.

[a] Approximately 21 percent of the panelists did not report the species of fish consumed. Approximately 6.1 percent of the panelists consumed other species of finfish.

[b] Numbers are rounded to two decimal places.

[c] The fish were sampled at source and are not samples of the fish consumed by the panelists.

probability of individuals exceeding an average daily intake of 30,000 ng Hg/70 kg body weight. It concluded that, under the previous FDA guideline of 500 ng Hg/g fish, 99.89 percent of the U.S. population would have a daily intake of less than 30,000 ng Hg/70 kg body weight. The report also estimated that 99.87 percent would be below this intake figure under the current FDA guideline of 1,000 ng Hg/g fish.

The National Academy of Sciences (1978) criticized the U.S. Department of Commerce Report (1978) because "consumption rates were figured at less than normal portions and at minimum mercury levels." They noted that Weight Watchers^R diet portions of fish are larger than the values of portions of fish used in the U.S. Department of Commerce (1978) study. McDuffie (1973) has reported intakes of mercury by 41 dieters in New York State. He reported that 25 percent consumed between 9 and 16 µg Hg/day, the second quartile between 17 and 26, the third quartile between 27 and 38, and the highest quartile from 40 to 75 µg Hg/day.

Given the difficulties in accurately estimating dietary intakes of mercury, it is surprising that no comprehensive surveys have been reported on blood concentrations of mercury in representative samples of the U.S. population. Goldwater (1964) reported on a study involving 15 countries and 1107 samples and found that concentrations of total mercury in blood were below 5 ng Hg/ml in 77 percent of the samples and below 10 ng Hg/ml in 89 percent of the samples. The Swedish Expert Group (1971) noted that blood concentrations in the general population in Sweden were influenced by fish consumption. Blood concentrations were in the range of <1 to 6 ng Hg/ml in people having low or zero fish consumption. High fish consumers, particularly those consuming large carnivorous oceanic fish, develop much higher blood concentrations. In McDuffie's study (1973) on Weight Watchers^R, two of the 41 dieters had maximum blood concentrations between 50 and 100 ng Hg/ml, which is consistent with a daily intake in the range 50 to 100 µg Hg (using the model discussed in the next section). Gowdy, et al. (1977) reported that 9 of 210 subjects whose blood was collected for health reasons showed total mercury levels above 50 ng Hg/ml, and 4 were above 100 ng Hg/ml. The form of mercury was not identified so that these high values may not have been due to the intake of methylmercury in fish. However, the relationship between inorganic and methylmercury may be more complicated than previously suspected because of a recent report on dentists in which methylmercury levels were found to be five times higher in dentists than in controls not exposed to inorganic mercury (Cross, et al. 1978).

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms. A number of attempts have been made to determine the BCF experimentally. Using mercuric chloride, Pentreath (1976a) found a BCF of about 250 for muscle of plaice (flounder). Kopfler (1974) obtained a value of about 10,000 for oysters.

The BCF has also been determined experimentally for methylmercury compounds. Tests with freshwater fish have obtained BCF values for methylmercury up to 8,400 for rainbow trout (Reinert, et al. 1974), 20,000 for brook trout (McKim, et al. 1976), and 63,000 for fathead minnows (Olson, et al. 1975) for a geometric mean of 22,000. For saltwater fish, a steady-state BCF of about 1,200 was predicted for the plaice (Pentreath, 1976a) and a value of 1,100 was found for skate (Pentreath, 1976b) for a geometric mean of 1,150.

Kopfler (1974) found that oysters achieved BCF values up to 30,000 for methylmercury, although many of the animals died in the 60-day exposure. No data are available concerning BCF values for decapods, but they would probably have values similar to those of saltwater fishes.

The wide range of BCF values obtained experimentally no doubt reflects the many practical and theoretical difficulties underlying such determinations. The factors governing methylmercury accumulation in fish are not completely understood but species, age of the fish (or length), position in the food chain, water temperature, the chemical form of mercury, are suspected as being important (for discussion, see Ottawa River Project, 1976). The chemical and physical species of mercury in various bodies of water will also vary with salinity, pH, etc. as discussed previously in this text.

Given the large number of variables involved and the wide range of experimentally determined BCFs, i.e., from 250 to 63,000, it would seem unrealistic to attempt to apply these values to the real conditions of fish exposure to mercury in natural waters. Instead, an attempt has been made to estimate a practical approximation to the true value of the average BCF. These practical approximations will be termed practical bioconcentration factors (PBCF). These values will be calculated as the ratio of the average concentration of mercury in muscle in one species of fish to the average concentration of mercury in the body of water in which the species normally lives. These values are listed in Table 7 for three bodies of water: freshwater, estuarine and coastal and open ocean waters. The species of fish chosen are that which are most frequently consumed in the USA, i.e., trout from freshwater, flounder and shrimp from estuarine and coastal waters, and tuna from open ocean waters (see Table 8). The PBCF are in the range 3,750 to 13,000.

These calculations depend upon a number of assumptions. The basic assumption is that, on the average, the concentration of methylmercury in fish muscle is related to the concentration of total mercury in water. This

TABLE 7

Estimate of Practical Bioconcentration Factors (PBCF) for the Most Frequently Consumed Fish Living in Different Bodies of Water

Water Body	Median Mercury Concentration[a] (µg/g)	Most frequently consumed fish		PBCF
		Species[b]	Mean mercury concentration[c] µg/l	
Freshwater	40	Trout	0.15[d]	3,750
Estuarine and Coastal	17	Flounder Shrimp	0.08	4,700
Ocean	15	Tuna	0.20	13,000

[a] For details see text

[b] The most frequently consumed species in that body of water see Table 8 and Cordle, et al. 1978

[c] Values taken from Table 8.

[d] Stanford Research Institute, 1975.

TABLE 8

Fish and Shellfish Consumption in the United States (September 1973-August 1974)*

	Rank	Amount, 10^6 lb/yr	Percent of total by weight	Number of Actual users (millions)	Mean Amount per user, g/day
Total		2957	100.	197	18.7
Tuna (mainly Canned)	1	634	21.4	130	6.1
Unclassified (mainly breaded, including fish sticks)	2	542	18.4	68	10.0
Shrimp	3	301	10.2	45	8.3
Ocean Perch[a]	4	149	5.0	19	9.7
Flounder	5	144	4.9	31	8.6
Clams	6	113	3.8	18	7.6
Crabs/lobsters	7	110	3.7	13	10.6
Salmon	8	101	3.4	19	6.7
Oysters/scallops	9	88	3.0	14	7.8
Trout[b]	9	88	3.0	9	12.3
Cod[a]	11	78	2.7	12	8.1
Bass[b]	12	73	2.5	7.6	12.0
Catfish[b]	12	73	2.5	7.5	12.1
Haddock[a]	12	73	2.5	11	8.6
Pollock[a]	15	60	2.0	11	6.8
Herring/smelt Sardines	16	54	1.8	10	6.7
Pike[b]	17	35	1.2	2.5	17.4
Halibut[a]	18	32	1.1	5.0	8.0
Snapper	18	32	1.1	4.3	9.3
Whiting	20	25	0.9	3.2	9.7
All other classified		152	5.1		

*Source: Cordle, 1978.

[a] Mainly imports.
[b] Fresh water.

might be true if (1) methylmercury on the average is a constant fraction of total mercury in water and (2) uptake of methylmercury either via the gills and from the food chain, depends ultimately on average methylmercury concentration in water. Studies on uptake of methylmercury by perch in the Ottawa River indicate that direct absorption via the gills is more important than uptake from the food chain (Ottawa River Project, 1976). The PBCF given in Table 7 will represent the overall average resulting from an interplay of the factors operative in that particular body of water. If a systematic change takes place in that body of water, the PBCF may also change. For example, acid rain may lead to acidification of freshwater. The lower pH leads to greater accumulation of mercury by fish (Jernelov, 1980) and thus increases the PBCF.

Inhalation

In 1934, Stock and Cucuel reported average air concentrations in the general atmosphere in Germany to be 20 ng Hg/m^3. Swedish and Japanese findings made 30 years later were similar (Fujimura, 1964; Eriksson, 1967). Sergeev (1967) reported concentrations averaging 10 ng Hg/m^3 in the USSR. McCarthy, et al. (1970), working in Denver has documented the lowest reported findings, 2 to 5 ng Hg/m^3. In the San Francisco area, concentrations were in the range of 0.5 to 50 ng Hg/m^3, according to Williston (1968).

Isolated "hot spots" having unusually high concentrations of mercury in the atmosphere have been reported near suspected points of emissions. For example, air levels of up to 10,000 ng Hg/m^3 near rice fields where mercury fungicides had been used and values of up to 18,000 ng Hg/m^3 near a busy superhighway in Japan have been reported by Fujimura (1964). Maximum air concentrations of 600 and 15,000 ng Hg/m^3 near mercury mines and refineries, respectively, were reported by McCarthy, et al. (1970). The highest reported levels of mercury in the atmosphere is reported Fernandez, et al. (1966) who found values of up to 800,000 ng Hg/m^3 in a village near a large mercury mine in Spain. The remarkably high mercury vapor levels reported by these authors indicate a need for further investigations into localized high concentrations of mercury in the atmosphere.

Many of these authors have suggested that elemental mercury vapor is the predominant form of mercury in the atmosphere (NAS, 1978). Observations by Johnson and Braman (1974) at a suburban site in Florida indicate that approximately 60 percent of the mercury in the atmosphere is in the form of vapor, 19 percent is inorganic, and 14.9 percent occurs as methylmercury compounds. Mercury present in a particulate form accounted for less than 1 percent. The amount of mercury bound to particulates seems to be related to area of industrialization and urbanization. For example, Heindryckx, et al. (1974) found that aerosol mercury levels corresponding to remote background levels in Norway and Switzerland were as low as 0.02 ng Hg/m^3. In a heavily industrialized area of Belgium near Liege the aerosol levels noted were as high as 7.9 ng Hg/m^3. In New York City (Goldwater, 1964) and Chicago (Brar, et al. 1969), concentrations of particulate-bound mercury of up to 41 and 14 ng Hg/m^3, respectively, were observed. However, as pointed out by the National Academy of Sciences (1978), considerable technical difficulties present themselves in the attempt to measure particulate-bound mercury; methods development and more reliable data are needed in this area.

The average concentration of mercury in the ambient atmosphere appears to be about 20 ng Hg/m^3. Assuming a daily ventilation of 20 m^3 for the "standard 70 kg man," and assuming that 80 percent of the inhaled vapor is retained, the average daily retention should be 320 ng Hg/70 kg body weight. In urban and industrialized areas, it seems unlikely that the mercury concentration in the atmosphere will regularly exceed 50 ng/m^3, corresponding to 800 ng Hg daily retention. The contribution of inhalation where people may be living near "hot spots" is impossible to assess without further information on air concentrations and the time of residence of individuals in these areas.

Occupational exposure to mercury vapor occurs in this country (Smith, et al. 1970). The current threshold limit for occupational exposures is 0.05 mg Hg/m^3. Assuming a ventilation of 10 m^3 during the working day, a 5-day per week exposure, and an average time-weighted air concentration which does not exceed 0.05 mg Hg/m^3, then the maximum daily retention from occupational sources should not exceed 2,800 µg/70kg for a 7-day week.

Dermal

In general, absorption of mercury through the skin is not a significant route of human exposure. However, under certain circumstances, such as occupational and medicinal exposure, it may be significant (see Absorption section).

PHARMACOKINETICS

The disposition of mercury in the body was reviewed by a Task Group on Metal Accumulation (1973) and more recently by a WHO Expert Committee (WHO, 1976). Since the disposition of mercury in the body is highly dependent upon the physical and chemical forms of this metal, it will be necessary in this section to consider them separately. Most information with regard to disposition in man and animals is available for methylmercury compounds and organic complexes of mercury ingested in the diet and for the inhalation of mercury vapor.

In general, insufficient information is available on other compounds of mercury, except for the mercurial diuretics, to allow an extensive discussion. Because mercurial diuretics are now virtually obsolete for therapeutic use, a complete review of this topic is not called for.

Nordberg (1976) and the Task Group on Metal Accumulation (1973) have reviewed evidence for suitable indicator media for methylmercury. The evidence reviewed below indicates that the blood concentration of methylmercury is a measure of the accumulation in the body and the concentration in the target organ, the brain. Urinary excretion is a poor indicator of body burden as most of the mercury is excreted via the feces. The hair is probably the indicator medium of choice as not only does it indicate current blood concentrations but also, depending upon the length of the hair sample, can give a recapitulation of past exposures.

Caution, however, should be observed in the proper use of these indicator media. There is still uncertainty as to whether the brain concentration exactly parallels the blood concentration in man. Secondly, the blood concentration could undergo a transient increase in individuals who have recently consumed a large amount of methylmercury. The hair sample has to be analyzed in a special way and has to be collected, transported, and stored under special conditions, as discussed by Giovanoli and Berg (1974), to avoid the appearance of artifacts.

There is no satisfactory indicator medium for assessment of mercury vapor exposure, body burdens, and concentration in the target organ. It is the practice in industry to use urinary concentrations on a group basis to give an indicator of exposures and body burden. However, it seems likely that urinary concentrations may reflect kidney levels rather than concentrations in the target tissue of the brain.

Since several exponential terms are required to describe the blood curve following a brief mercury vapor, multicompartment pharmacokinetics are implied for man. Thus, an isolated blood sample will not provide any information regarding exposure or body burden. Serial samples, however, may indicate the existence of a steady state or give limited information about recent exposure. If individuals are in steady state, correlation between time-weighted average air concentrations and blood concentration should be expected. This was confirmed by Smith, et al. (1970) in chronically exposed workers. The authors observed about a 49 µg/100 ml increase in the steady-state blood level for each 1 mg/m^3 increase in the blood exposure concentration.

The same considerations with regard to indicator media apply to inorganic mercury as to inhaled mercury vapor. It is likely that urinary mercury excretion primarily reflects the accumulated amount in kidney tissue. Conclusions about the role of blood as an indicator medium cannot be made, since little is known about the biological halftimes of mercury in the blood compartment versus other tissues.

Absorption

Methylmercury and Other Short Chain Alkyl Mercurials: No quantitative information is available on the absorption of the short-chain alkyl mercurial compounds through human skin. However, cases of severe poisoning have occurred following the topical application, for medicinal purposes, of methylmercury compounds (Tsuda, et al. 1963; Ukita, et al. 1963; Okinata, et al. 1964; Suzuki and Yoshino, 1969). Although, in these cases, the main pathway of intake was probably through skin, the possibility of some inhalation exposure cannot be excluded.

Likewise, no specific data are available on the inhalation of alkyl mercurial compounds. The Task Group on Metal Accumulation (1973) suggested that the retention of the inhaled mercurials would probably be on the order of 80 percent. These conclusions were based mainly on the diffusibility and the lipid solubility of many of the compounds of methylmercury. Furthermore, no quantitative information is available on dusts and aerosols of the alkyl mercurial compounds. Many of these compounds have been used in the past as fungicides, resulting in occupational exposures of workers. Since some of these occupational exposures have led to severe poisoning and death, it seems likely that lung retention would be high, although both skin absorption and gastrointestinal absorption might also have played a role.

Several quantitative measurements have been made on the absorption of methylmercury compounds in the gastrointestinal (GI) tract. Experiments on volunteers by Aberg, et al. (1969) and Miettinen (1973) have demonstrated virtually complete absorption in the GI tract whether the methylmercury is administered as a simple salt in solution or whether it is bound to protein. The findings of the tracer studies have been confirmed in observations of volunteers who ingested tuna fish for several days (Turner, et al. 1974, 1975). Shahristani and coworkers (1976), in studies of the dietary intake of methylmercury in homemade bread contaminated with a fungicide, obtained results consistent with a high degree of absorption from the diet.

No quantitative information is available on the other short-chain alkyl mercurials. However, the fact that several outbreaks of poisoning have occurred due to the consumption of homemade bread contaminated with ethylmercury fungicides suggests that this form of mercury is also well absorbed from the GI tract.

Age and sex differences in GI absorption of methylmercury compounds have not been reported. However, the fact that very high blood concentrations of methylmercury were attained in infants who had ingested methylmercury solely in their mothers' milk suggests that absorption in the very young is substantial (Amin-Zaki, et al. 1974b).

Mercury Vapor and Liquid Metallic Mercury: About 80 percent of inhaled mercury vapor is retained as evidenced by observations of humans (Teisinger and Fiserova-Bergerova, 1965; Neilsen-Kudsk, 1965a; Hurch, et al. 1976). Teisinger and Fiserova-Bergerova (1965) proposed that the vapor was absorbed across the walls of the bronchioles and larger airways of the lung, but subsequent evidence points strongly to the alveolar regions as the predominant site of absorption into the blood stream (Berlin, et al. 1969).

The importance of skin as a pathway for transport of metallic mercury into the blood stream is debatable. Juliusberg (1901) and Schamberg, et al. (1918) indicated that appreciable skin absorption of metallic mercury takes place in animals. However, the possibility cannot be excluded that some inhalation exposure also occurred in these experiments.

The gastrointestinal absorption of metallic mercury in the liquid form is believed to be very small. Bornmann, et al. (1970) administered gram quantities orally to animals, and Friberg and Nordberg (1973) calculated that less than 0.01 percent of the administered dose of metallic mercury was in fact absorbed. Persons have accidentally ingested several grams of metallic mercury and showed some increase in blood levels (Suzuki and Tonaka, 1971). However, there are many case reports in the literature of individuals consuming, accidentally or otherwise, gram quantities of liquid metallic mercury and the metal passing through the GI tract into the feces without any ill effects.

Salts of Inorganic Mercury: No quantitative information is available on the absorption of mercury in the form of inorganic mercuric (Hg^{++}) salts by human skin. However, solutions of mercuric chloride have been shown to be absorbed by guinea pigs; 5 percent of the mercury in a 2 percent solution of mercuric chloride was absorbed across the intact skin of these animals over a 5-hour period (Friberg, et al. 1961; Skog and Wahlberg, 1964). If such a rate of penetration applied to human skin, one might expect substantial absorption of mercuric chloride salts in man.

Information on the pulmonary deposition and absorption of inorganic mercury aerosols is lacking except for the experimental work on dogs by Morrow, et al. (1964). This group reported that 45 percent of mercury administered as mercuric oxide aerosol having a mean diameter of 0.16 µm was cleared within 24 hours; the remainder cleared with a halftime of 33 days.

Rahola, et al. (1971) reported findings on the GI absorption of inorganic mercury given to ten volunteers. Eight of the volunteers, five males and three females, received a single dose of mercuric nitrate bound to calf liver protein, containing approximately 6 µg of inactive mercury per dose. The other two volunteers received an acid solution of mercuric nitrate. During the 4 to 5 days following treatment, an average of 85 percent of the dose was excreted in the feces; urinary excretion was only 0.17 percent of the dose. These findings suggest that GI absorption of inorganic mercury by humans is less than 15 percent, which correlates with studies on experimental animals (Clarkson, 1971). Experiments on animals indicate that GI absorption is greater in suckling animals than in mature ones (Kostial, et al. 1978).

Other Compounds of Mercury: The aryl and alkoxy-aryl mercurials are used as fungicides and slimicides, and as such occupational exposures to these compounds probably still occur. To what extent these mercurials reach the water supply is not known. In general, the aryl mercurials are well absorbed from the GI tract, as evidenced by animal experiments (Clarkson, 1971). Most classes of these organo-mercurial compounds undergo rapid conversion to inorganic mercury in body tissues.

Distribution and Metabolism

Methylmercury and Other Short-Chain Alkyl Mercurials: Details on the distribution and retention of methylmercury in man and animals were reviewed by Friberg and Vostal (1972), by the Task Group on Heavy Metal Accumulation (1973), and by a WHO Expert Committee (1976). The general picture which emerges is that methylmercury compounds, after absorption from the GI tract, distribute readily to all tissues in the body. Unlike inorganic mercury, large concentration differences in various tissues are not seen. Methylmercury is characterized by its ability to cross diffusion barriers and cell membranes without difficulty.

Tracer studies in volunteers have revealed that about 5 percent of the ingested dose is deposited in the blood compartment after tissue distribution is completed. About 90 percent of the methylmercury in blood is associated with the red blood cells. Thus, the red cell to plasma ratio is between 10 to 1 and 20 to 1. The mercury in the red blood cells is almost entirely (more than 90 percent) in the form of methylmercury compounds. However, in plasma approximately 25 percent can be in the form of inorganic mercury that has been produced by cleavage of the carbon-mercury bond (Bakir, et al. 1973). The rate of decline in blood concentration of methylmercury after cessation of exposure can be well described by a single biological halftime as evidenced by both tracer experiments in volunteers and also in people who had ingested methylmercury in substantial amounts from either fish or contaminated food (see Table 9). The tracer experiments reveal a halftime of approximately 50 days. However, the range of halftimes reported in both tracer experiments and in people having substantial exposures covers a wide range. Whether this range of values is due to individual differences or to experimental or observational inaccuracies in the measurements is not clear.

Based on observations in animals, the entry of the mercury into the brain is delayed by a few days as compared to entry into other tissues (Norseth and Clarkson, 1971). According to observations on volunteers, the amount transferred to the head region following the ingestion of a single dose of radioactive tracer is about 10 percent of the body burden after tissue distribution is complete. However, only three subjects were involved in this study (Aberg, et al. 1969). There is a great need for more data which would allow estimation of the amount of mercury that enters this critical organ (the brain). In man, the brain to blood ratio is in a range of 5 to 1 or 10 to 1. The biological halftime of methylmercury in the brain is not well described in man, but the observations by Aberg, et al. (1969) of three volunteers indicate a halftime in roughly the same range as that observed in blood and in the whole body (Table 9). Whether or not the halftimes in brain and blood are identical is an important consideration in the decision to use blood as an indicator medium for brain concentrations.

The concentration of methylmercury in other tissues such as muscle, liver, and kidney usually does not vary by more than a factor of 2 or 3, with the highest concentrations being found in the kidney cortex. In muscle, the mercury is usually almost entirely in the form of methylmercury, but in liver and kidney a substantial proportion can be present as inorganic mercury. Most of this evidence is based on studies using animals. Autopsy data in Iraq indicate a substantial proportion present as inorganic mercury in the liver (Magos, et al. 1976).

TABLE 9

Mercury Intake and Biological Halftimes

No. of subjects	Hg intake (µg/kg/day)	Halftimes (days)			References
		Body	Blood	Hair	
5	trace	70[a]	--	--	Aberg, et al. (1969)
15	trace	76 (52-93)[b]	50	--	Miettinen (1973)
5	up to 5	--	--	(33-120)	Birke, et al. (1967)
5	up to 5	--	-- (58-164)[c]	--	Skerfving, et al. (1974)
16	up to 50	--	65 (45-105)	--	Bakir, et al. (1973)
48	up to 50	--	--	72[d] (35-189)	Shahristani and Shihab (1974)

[a] Mean

[b] Range

[c] One person had a biological halftime of 164 days. The other four were in the range of 58-87 days.

[d] The data were distributed bimodally. One group accounting for 89 percent of the samples had a mean value of 65 days and the other group had a mean value of 119 days.

Methylmercury is readily transferred from mother to fetus across the placenta. At birth the concentration in the umbilical cord or infant blood is usually slightly higher than that observed in maternal blood. In observations of women having normal pregnancies and on a low to moderate fish intake, Tejning (1970) reported that methylmercury in the fetal blood cells was about 30 percent higher than in the maternal cells. Suzuki, et al. (1971) confirmed the finding of higher fetal blood concentrations. The studies on the outbreak of methylmercury poisoning in Iraq (Bakir, et al. 1973; Amin-Zaki, et al. 1974a, 1976) also showed that methylmercury was readily transferred across the placenta, resulting in higher concentrations in fetal blood at the time of delivery. Apparently the differences between fetal and maternal blood are due to differences in concentration in the red blood cells rather than to differences in plasma concentrations.

Methylmercury is secreted in mother's milk. The studies of the Iraqi outbreak revealed the close correlation between maternal milk and blood concentrations, with the milk concentration on the average being about 5 percent of the simultaneous blood concentration (Bakir, et al. 1973). About 40 percent of the mercury in milk was found to be in the inorganic form. Skerfving, et al. (1974), in a study of 15 lactating females following intake of methylmercury from fish, also noted a correlation with blood concentrations but found a smaller percentage (approximately 20 percent) of mercury in the form of methylmercury in the milk.

Mercury is accumulated in head hair after exposure to methylmercury compounds. A variety of observations (Table 10) indicate that the hair to blood concentration ratio is about 250 to 1 with considerable variation from one study to another. Mercury is accumulated in the hair at the time of its formation and thus, in freshly formed hair, the concentration in hair is proportional to that in blood. Once incorporated into the hair sample the

TABLE 10

Relationship between Concentrations of Mercury in Samples of Blood and Hair in People having Long-term Exposure to Methylmercury from Fish*

No. of subjects	Whole blood (x) (mg/kg) range	Hair (y) (mg/kg) range	Linear regression
12	0.004 - 0.65	1 - 180	$y = 280x - 1.3$
51	0.004 - 0.11	1 - 30	$y = 230x + 0.6$
50	0.005 - 0.27	1 - 56	$y = 140x + 1.5$
45	0.002 - 0.80	20 - 325	$y = 260x + 0$
60	0.044 - 5.5	1 - 142	$y = 230x - 3.6$

*Source: WHO, 1976

concentration of mercury is stable and thus, as the hair is examined longitudinally, a history is obtained of previous blood concentrations (Clarkson, et al. 1976). Hair grows at approximately 1 cm per month (Shahristani and Shihab, 1974) so that the measurement of each 1 cm segment corresponds to the average blood concentration during a particular month. The hair is therefore a very useful medium to recapitulate past exposures as well as to give information on current exposure to methylmercury. An example of the close parallel between concentration in hair and blood is shown in Figure 2 (Amin-Zaki, et al. 1976).

Methylmercury is metabolized to inorganic mercury in animal tissues (Gage, 1961; Norseth and Clarkson, 1970). In man, conversion to inorganic mercury is an important process in excretion, as shall be discussed later.

Mercury Vapor and Liquid Metallic Mercury: Approximately 2 percent of an inhaled dose of radioactive mercury vapor was found to be deposited in 1 liter of whole blood after tissue distribution was complete (Hurch, et al. 1976). The concentration in the red blood cells of these volunteers was higher than that seen in plasma. The halftime in blood was estimated to be about 4 days, accounting for at least 60 percent of the mercury deposited in the blood volume.

An accidental mercury vapor exposure of a family has supplied some additional information concerning halftimes (Figure 3). The major portion of the exposure probably occurred within a half-hour period with a smaller protracted exposure over the duration of an evening. It appears that there was an early rapid decline over the first few days postexposure, and by about 5 to 7 days, the mercury in blood was decreasing with an approximate 15-day halftime which was maintained for the remainder of the first month's postexposure. Another family's exposure to mercury vapor involved a husband and daughter who were exposed for 6 to 8 months in the home. The wife had experienced a prior exposure for about 18 months in her workplace. Samples of

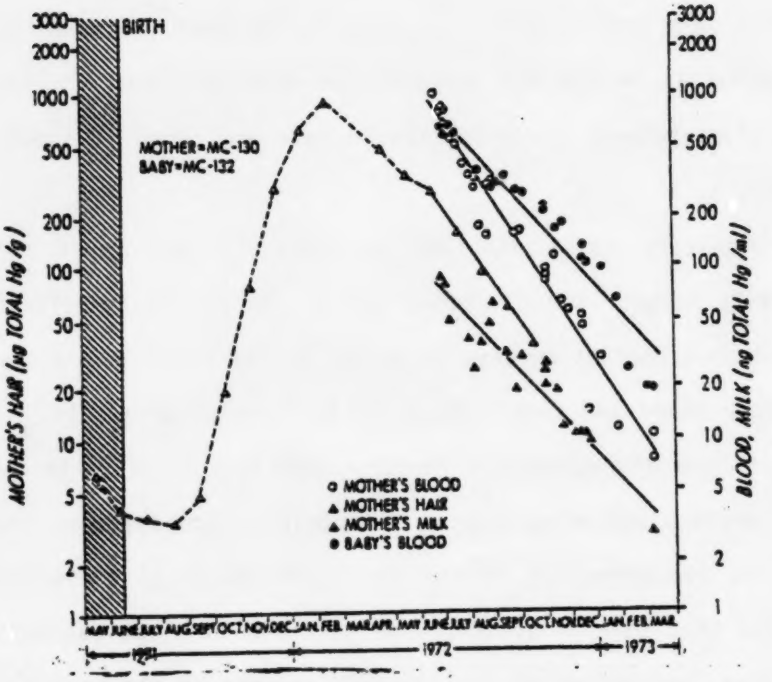

FIGURE 2.

Concentration of total mercury in 1 cm segments of sample of mother's hair, whole blood, and milk, and baby's blood(postnatal exposure). Concentrations in milk and blood are plotted according to dates of collection.

Source: Amin-Zaki, et al. 1976.

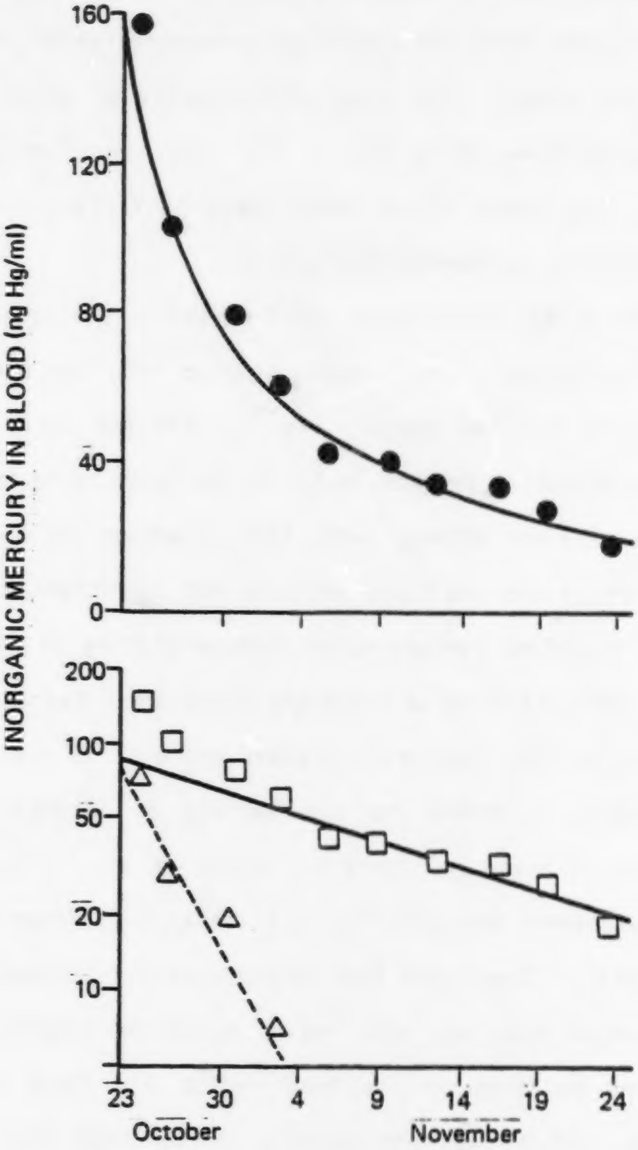

FIGURE 3.

The fall in mercury concentrations in blood in two adult females following a brief exposure (less than 3 hr) to mercury vapor. Upper graph has a linear scale on the ordinate. The lower graph has a logarithmic scale and curve feathering procedures were used to estimate a component with the different halftime (slow component, 14.9 days; fast component, 2.4 days).

Source: Clarkson, 1978.

blood were collected starting about one month after cessation of exposure. Therefore, an early and rapid fall in blood concentration due to short halftime components was missed. The blood concentration of mercury in the wife declined, with a halftime of 30 days. The other two family members had longer halftimes, but their blood levels were sufficiently low that dietary mercury might have influenced the results.

Evidence from animal experiments and from isolated suspensions of human blood indicate that mercury vapor, once absorbed into the bloodstream, can undergo oxidation to divalent mercury (Hg^{++}). The red cells are an important site of this oxidation process, which is believed to be mediated by the hydrogen peroxide catalase pathway (WHO, 1976; Clarkson, et al. 1978). However, the oxidation in the red blood cells is not sufficiently rapid to prevent some of the dissolved mercury vapor from persisting in the blood stream for sufficient periods of time to reach the blood-brain barrier. Here it is believed to cross rapidly into brain tissues where it is again subjected to oxidation processes. A scheme for the pathway of inhaled mercury vapor reaching the brain is given in Figure 4. Hurch, et al. (1976) made regional body counts on volunteers who had (Figure 4) inhaled a tracer dose of radioactive mercury vapor. They found that approximately 7 percent of the inhaled dose was absorbed into the head region following completion of tissue distribution. The halftime in the head region was found to be 21 days (Table 11). This halftime was considerably shorter than that seen in other tissues in the body with the exception of blood.

The main site of accumulation of mercury in the body after inhalation of mercury vapor is the kidney. In fact, animal experiments indicate that as much as 90 percent of the total body burden can be found in kidney tissues (Rothstein and Hayes, 1964).

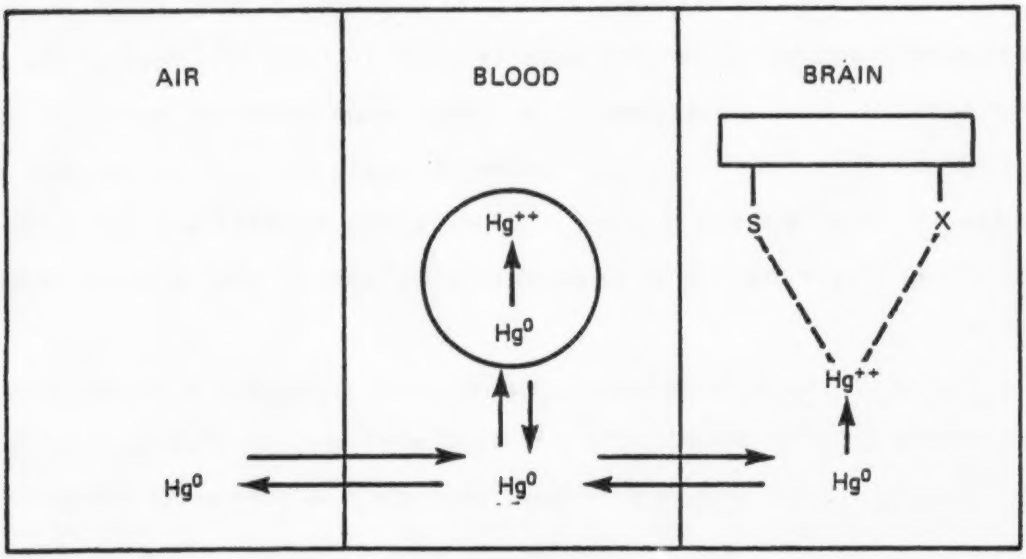

FIGURE 4.

A diagrammatic representation of the pathway of inhaled mercury vapor (Hg^0) to the brain. The oxidation process (Hg^0 Hg^{++}) is depicted as occurring in the red blood cells and brain tissue. Oxidation also occurs in other areas. The ligands to which Hg^{++} attaches have not been identified (depicted as S and X) but sulfhydryl groups are suspected to be involved.

Source: Clarkson, 1974.

Mercury can penetrate into the fetus after maternal exposure to mercury vapor. This rate of transfer appears to be considerably greater than that seen for the inorganic species of mercury (Clarkson, et al. 1972). However, no published information is available with regard to human exposures. Observations of a family accidentally exposed for a brief period of time to mercury vapor indicated that the mercury concentration at delivery of the baby was the same as that in the mother.

A summary of the estimated biological halftimes of mercury in the body following exposures to mercury vapor is given in Table 11. Most of the information in this table comes from tracer experiments of Hurch, et al. (1976) and from unpublished observations of people who were accidentally exposed for brief periods of time. The whole-body halftime and the halftime in kidney tissue seem to be approximately the same as that of methylmercury in man.

Salts of Inorganic Mercury: Studies using a variety of animal species have shown that, in general, the distribution of mercury after doses of mercuric salts or inorganic mercury bound to protein is similar to the distribution observed after exposure to mercury vapor (Clarkson, 1972a, b; Friberg and Vostal, 1972). However, there are important differences. The red cell to plasma ratio has been reported to be 0.4 in humans exposed to a tracer dose of Hg^{++} (Rahola, et al. 1971), whereas the amount in the red cells is considerably higher after exposure to mercury vapor (Cherian, et al. 1978). The most dramatic differences lie in the ability to penetrate across the blood-brain and placental barriers. Relatively small amounts of the mercuric ion penetrate the brain or the fetus following exposure to inorganic salts as compared to mercury vapor and alkyl mercury compounds. Jogo (1976) has reported that the blood-brain barrier of suckling rats is more permeable to inorganic mercury than that of adults.

TABLE 11

Summary of Halftimes of Mercury in Human Tissues

Tissue	Exposure		First Component		Second Component	
	Conc. mg/m^3	Duration	Percent Deposited	t 1/2 days	Percent Deposited	T 1/2 days
Blood[a]	0.1	20 min	60	4.0	not detected	
Blood[b]	0.1	few hours	90	2.0	10	14.9
Blood[b]	0.05	months	d	d	100	30
Lung[c]	0.1	20 min	100	1.7	not detected	
Kidney[c]	0.1	20 min	100	64.0	not detected	
Head[c]	0.1	20 min	100	21.0	not detected	
Whole Body[c]	0.1	20 min	100	58.0	not detected	

[a] Cherian, et al. 1978
[b] Clarkson, 1978. For details, see text.
[c] Hurch, et al. 1976.
[d] Not measured

Inorganic Mercury Accumulation in the Kidneys: Animal experiments have shown that as much as 90 percent of the body burden can be found in this organ. Inorganic mercury has the ability to induce the synthesis of metallothionein or metallothioneinlike proteins in kidney tissue (Piotrowski, et al. 1974a, 1974b). This ability is shared with inhaled mercury vapor (Cherian and Clarkson, 1976).

The retention of mercury by five human volunteers after a single dose of inorganic mercury has been reported by Rahola, et al. (1971). The whole-body biological halftime averaged 45 days and was significantly greater than the biological halftime observed for plasma (24 days) or for the red blood cells (28 days). Rahola, et al. (1971) reported that 0.2 to 0.4 percent of the ingested dose was found in the blood volume 1 day after dosing.

Other Compounds of Mercury: The conversion of organomercurial compounds to inorganic mercury results eventually in a pattern of distribution that is similar to that obtained after exposure to inorganic salts. The kidney is the main organ of accumulation in all cases.

Excretion

Methylmercury and Other Short-Chain Alkyl Mercurials: The excretion of mercury from the body in humans exposed to methylmercury occurs predominately by the fecal route. Less than 2 percent of excretion occurs in the urine. The form of mercury in feces is almost completely the inorganic form (Turner, et al. 1974), and about 90 percent of the mercury in urine is also inorganic (Bakir, et al. 1973). These observations indicate that, in man, an important step in the excretion process is the cleavage of the carbon-mercury bond.

The site of the cleavage of this carbon-mercury bond in the body is not known. Animal experiments indicate there is a substantial biliary secretion of methylmercury raising the possibility that biotransformation to the inorganic form might be affected by microflora in the gut (Norseth and Clarkson, 1971).

Mercury Vapor and Liquid Metallic Mercury: Urine and feces are the main pathways of excretion after exposure to mercury vapor, although exhalation of vapor and excretion in saliva and sweat may contribute (Lovejoy, et al. 1974; Joselow, et al. 1968). Animal data indicate that, shortly after exposure, the GI tract is the predominant pathway of excretion, but as the kidney becomes more and more the predominant site of storage of mercury, urinary excretion takes over (Rothstein and Hayes, 1964). In humans, following a brief exposure, urine accounted for 21 percent of the total urine and fecal excretion, but after a long-term occupational exposure, urine contributed 58 percent (Table 12). Tracer experiments using human volunteers indicated that the specific activity of mercury in urine was unrelated to the specific activity in plasma (Cherian, et al. 1978). This observation suggests that urinary mercury originates from a large pool of mercury in the kidney rather than from glomerular filtration of plasma mercury.

Approximately 7 percent of an inhaled dose of mercury vapor was shown to be excreted in the expired air of humans. The majority of this was expired within seven days and comprised 37 percent of the first week's excretion (Table 12).

Quantitative information on the excretion via sweat and saliva is not available. In workers experiencing profuse perspiration, amounts of mercury excreted in the sweat may exceed those of urine (Lovejoy, et al. 1974).

High individual variation and great day-to-day fluctuation were the principal features of urinary mercury excretion by workers under similar exposure conditions (Jacobs, et al. 1964). Copplestone and McArthur (1967)

TABLE 12

Parameters of Excretion of Mercury in Man Following Exposure to Mercury Vapor

Excretion Medium	Exposure		Percent of Total Observed Excretion
	Conc. (mg Hg/m^3)	Duration	
Urine	0.1	20 minutes	13[a]
Urine	0.05 - 0.2	(years)	58[b]
Feces	0.1	20 minutes	49[a]
Feces	0.05 - 0.2	(years)	42[b]
Expired air	0.1	20 minutes	37[a]

[a] Average excretion during first week after exposure (Hurch, et al. 1976; Cherian, et al. 1978).

[b] Combined urine and feces (Tejning and Ohman, 1966).

found no correlation between urinary excretion and air concentrations. They noted that some individuals excreted extremely large amounts of mercury, some in excess of 1,000 µg/l without apparent ill effects. Their own findings and their review of the literature (Jacobs, et al. 1964; Neal, et al. 1941) led Copplestone and McArthur (1967) to propose that "mercurialism might be due to an inability to excrete absorbed mercury rather than simply to exposure."

Piotrowski, et al. (1973) observed workers following exposure to mercury vapor, and reported that urinary excretion could be described by a two-term exponential equation equivalent to halftimes at 2 and 70 days. The authors claimed that individual variations in urinary excretion are minimized when urine samples are collected at the same time each morning.

Lundgren, et al. (1967), Smith, et al. (1970), and Hernberg and Hassanan (1971) have reported generally similar relationships between steady-state urinary excretion and blood levels. Averaging their results, one would expect a 0.06 mg/l increase in the urinary excretion rate for each 1 µg/100 ml change in the blood mercury level. These results can be combined with the data on blood levels versus exposure concentration reported by Smith, et al. (1970) to predict a 2.9 mg/l change in the urinary excretion for each 1 mg/m^3 change in the time-weighted air concentration.

Tejning and Ohman (1966) cited steady-state urine and fecal excretion rates which can be interpreted to mean that urinary excretion will account for approximately 57 percent of combined urinary and fecal excretion when the exposure concentration is between 0.05 and 0.2 mg/m^3. When these excretion rates are compared to those predicted above, a discrepancy of a factor of 2 to 3 is found, with the predicted rates being greater than those observed by Tejning and Ohman (1966).

Several factors might contribute to the daily variability of urinary mercury concentrations. Daily changes in urinary specific gravity, problems with analytical methodology, volatilization of mercury from urine (Magos, et al. 1964), adsorption of mercury to glassware, the diffusion of mercury out of plastic bottles, and the entrainment of mercury into the particulate fraction of urine, all make the analysis of urinary mercury extremely difficult (Greenwood and Clarkson, 1970).

In conclusion, although correlation of urine mercury concentrations with blood or time-weighted air concentrations may yield consistent results when the data from large groups of people are averaged, there is no explanation is at hand for the large fluctuations in daily excretion by individuals. However, few longitudinal studies have been made, and all measurements to date on exposed workers with one exception have measured concentrations of total mercury. Recently, Henderson and coworkers (1974) have pointed to the importance of identifying chemical forms of mercury in urine. They concluded that dissolved elemental vapor in urine might be a better indicator than total mercury.

The exhalation of mercury in expired air is a recent finding in humans (Hurch, et al. 1976). The short halftime reported by these workers following brief exposure to the vapor suggests that mercury in expired air would indicate only recent exposure. However, experiments on animals given mercuric salts (Clarkson and Rothstein, 1964; Dunn, et al. 1978) reported a close correlation between the rate of exhalation and the body burden of divalent mercury (Hg^{++}). During chronic exposures to mercury vapor, the body burden of Hg^{++} may reach levels at which reduction of this form of mercury can make a significant contribution to loss by exhalation. Thus, sampling of expired air at appropriate times after inhalation of vapor may provide information on both recent and long-term exposure.

Salts of Inorganic Mercury: Studies by Rahola, et al. (1971) on volunteers who ingested tracer doses of inorganic mercury revealed that urine and fecal excretion were approximately equal after the unabsorbed oral dose was cleared by the GI tract. The whole body halftime of 45 days observed in these volunteers is consistent with excretion in urine and feces, amounting to a total of 1.5 percent of the dose per day.

It is possible that urinary excretion could be increased by kidney damage. For example, Cember (1962) reported that cytotoxic doses of inorganic mercury could lead to desquamation of renal tubular cells, resulting in a sharp increase in mercury excretion. Magos (1973) has reviewed other studies where agents producing kidney damage leading to desquamation of cells cause an increase in urinary mercury excretion.

Other Compounds of Mercury: Retention halftimes of the aryl and alkoxy-aryl mercurials in man are generally not known. Their rapid conversion to inorganic mercury would suggest that their halftimes would not exceed those reported in volunteers discussed earlier. The mercurial diuretics generally have halftimes considerably shorter than that reported for inorganic mercury because of the rapid excretion of the intact mercurial.

Mathematical Models of Accumulation of Methylmercury in Man: The body will continue to accumulate methylmercury so long as intake is greater than excretion until a steady state is obtained where intake and excretion balance. A common way to describe the progress of accumulation in the body is in terms of the biological halftime. This concept is useful, provided that the processes of transport and distribution in the body occur more rapidly than the elimination step. Thus, the single biological halftime can then describe the decline in not only the amount in the body but also in the concentration in various tissues. As pointed out by the WHO Expert Committee (1976), if tissue compartments retain mercury with widely differing retention halftimes, then the whole-body biological halftime would not be useful and could give misleading toxicological information.

However, this evidence indicates that the rate of decline of mercury in the whole body and in various tissues including the target organ can be described by a single biological halftime.

The WHO Expert Committee has summarized the mathematical expressions relating daily intake to biological halftime and accumulation in man. These derivations are quoted below.

In cases where the elimination of a metal such as methylmercury follows a single exponential first order function, the concentration in an organ at any time can be expressed by the following equation:

$$C = C_0 e^{-bt} \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where: C = concentration in the organ at time t

C_0 = concentration in the organ at time zero

b = elimination constant, and

t = time.

The relation between the elimination constant and the biological halftime is the following:

$$T = \frac{\ln 2}{b}$$

where: T = biological halftime, and

$\ln 2$ (natural logarithm of 2) = 0.693

If data on exposure and absorption of the metal are known, then it is possible to predict the body burden of the metal at constant exposure over different time periods. If a constant fraction of the intake is taken up by a certain organ, the accumulated amount in that organ can also be calculated. The following expression gives the accumulated amount of metal in the total body (or organ):

$$A = (a/b)\,(1-e^{-bt}) \quad \ldots\ldots\ldots\ldots\ldots\ldots (2)$$

where: A = accumulated amount, and

a = amount taken up by the body (or organ) daily.

At steady-state the following applies:

$$A = a/b. \dots\dots\dots\dots\dots\dots\dots\dots (3)$$

In other words, the steady-state amount in the body (or organ) A is proportional to the average daily intake and inversely proportional to the elimination rate. The latter point will be discussed in a later section in relation to human hazards, as large individual variations in elimination rates imply large individual variations in steady-state body burden, even in people having the same average daily intake.

Equations (1), (2), and (3) are illustrated graphically in Figure 5. During the period of steady daily intake (assumed to be 10 µg/70 kg body weight), the amount in the body rises rapidly at first, reaching half its maximum (steady-state) value in a time equivalent to one elimination halftime (assumed to be 69 days for methylmercury in man). After an exposure period equivalent to five elimination halftimes (approximately one year for methylmercury), the body is within 3 percent of its final steady-state value. The steady-state body burden is 100 times the average daily intake assuming an elimination halftime of 69 days. Upon cessation of exposure, the body burden will immediately begin to fall, following an exponential curve that is an inverse image of the accumulation curve. Thus the body burden will have returned to within three percent of pre-exposure values in five halftimes.

In this example, it is assumed that the hair-to-blood ratio is constant and equal to 250 and that 1 percent of the body burden is found in 1 liter of blood in a 70 kg man.

Equation 3 is useful in that it predicts a relationship between long-term dietary intake and the concentrations of mercury in such indicator media as blood and hair. It is thus possible to test the predictive value

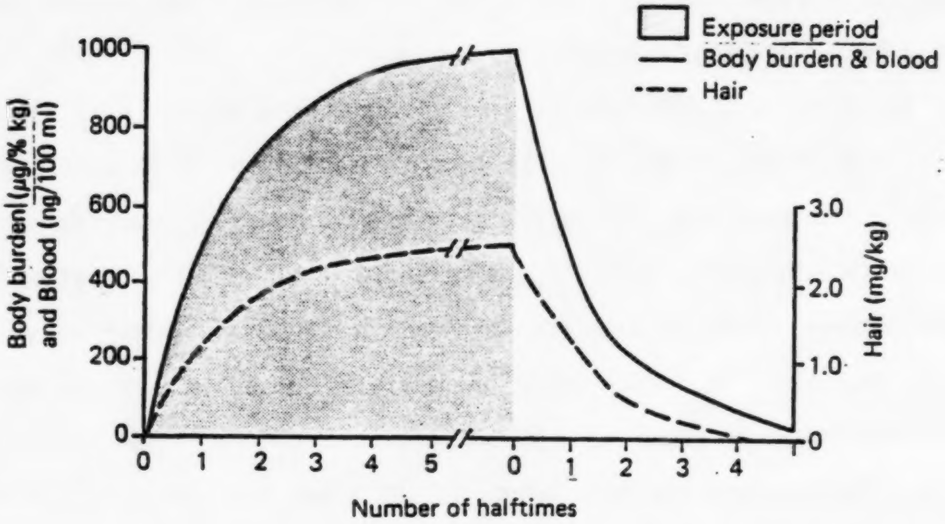

FIGURE 5.

The changes in the body burden and hair and blood concentrations of mercury during constant daily exposure (shaded area) and after exposure. This calculation was based on a daily intake of 10 µg of methylmercury during the exposure period, an elimination halftime of 69 days, and a hair to blood concentration ratio of 250.

Source: WHO, 1976.

of equation 3 by carrying out dietary studies on exposed populations and measuring concentrations of methylmercury in blood and hair. A prediction of equation 3 is that once the individual has attained steady state, the concentration in blood should be directly proportional to the average daily intake. This prediction was confirmed in a study by Skerfving, et al. (1974) in a group of fish eaters in Sweden. Results of Skerfving's study, along with studies on other fish-eating populations, are summarized in Table 13. In some cases, observations were made on concentrations in hair, and in others, measurements of blood concentrations were made. All have been converted into blood concentrations for comparative purposes. Furthermore, it is possible to predict the steady-state concentration in blood from a given dietary intake with the kinetic parameters given in the studies by Aberg, et al. (1969), and Miettinen (1973) on volunteers. This estimate is also given in Table 13. The calculation involves the assumption that 95 percent of the methylmercury was absorbed from the diet, that 1 percent was distributed in 1 liter of blood, and that the biological halftime in blood was approximately 50 days. In general, the factor relating the steady-state blood concentration to the average daily intake (the coefficient of x; Table 13) varies from a value of 0.3 to 1.0. The low values for this coefficient have been attributed to the difficulty of an accurate estimate of dietary intake and to the possibility that in some of the populations studied the individuals had not attained a true steady state. Nevertheless, equation 3 seems to be useful in that it allows comparison of the results of various types of studies, including both exposed populations and volunteers. A recent study of five volunteers ingesting contaminated freshwater fish yielded a coefficient of about 0.8, close to the tracer prediction of 1.0 (Kershaw, et al. 1978). Quantitative accuracy in relating dietary intake to steady-state blood levels is of considerable importance to estimates of hazard to human health from dietary intake of methylmercury.

TABLE 13

Relationship of Steady-State Blood Concentrations to Daily Intake of Methylmercury[a]

No. of subjects	Time of exposure	Avg. Hg intake (μg/day/70 kg Body Weight)	Steady blood concentration (ng/ml)
		(x)	(y)
6+26[b]	years	0-800	y=0.7x + 1
139+26[b]	years	0-400	y=0.3x + 5
6+14[b]	years	0-800	y=0.8x + 1
725[c]	years	0-800	y=0.5x + 4
22	years	0-800	y=0.5x + 10
15	single tracer dose		y=1.0x

Source: WHO, 1976

[a] For details of these calculations, see text.

[b] Little or no fish consumption in this group.

[c] Estimated from data on hair concentrations and daily intake. The hair to blood concentration ratio was assumed to be 250 and the average body weight of the population under study to be 60 kg.

Thus far, the discussions have employed average values for various parameters used in mathematical modeling of accumulation of methylmercury in man. In fact, there are substantial differences. The biological halftime in man, as indicated in Table 11, actually varies over a wide range of values. Shahristani and Shihab (1974) have published the observation that there is a bimodal distribution of biological halftimes as calculated from analysis of hair samples in the Iraqi outbreak. As shown in Figure 6, these authors found that the majority of a population of 48 people studied had halftimes distributed around the normal value of about 65 days, but about 9 percent of the population had a significantly different distribution of halftimes, averaging about 119 days. Greenwood, et al. (1978) have noted that the halftime in blood of lactating females (average 42 days) is significantly lower than that of nonlactating adult females (average 74 days). The excretion of methylmercury in milk is not sufficient to explain the reduced biological halftime in blood of lactating females.

Experiments on mice by Doherty, et al. (1977) have revealed that methylmercury is not eliminated from mice throughout their suckling period. Observations by Landry, et al. (1978) revealed that changes in the diet of mice can also lead to large changes in the biological halftime of methylmercury.

There are important species differences in the kinetics and distribution of methylmercury. For example, the blood to plasma ratio, which is about 10 to 1 for man and other primates, is as high as 300 to 1 in rats. The blood to brain ratios exhibit substantial species differences with man and other primates having a ratio of about 1 to 5, most laboratory animals having ratios of 1 to 1, and the rat having a ratio of 10 to 1. The biological halftimes may be as short as seven days in the mouse or as high as 700 days or more in certain marine species (Clarkson, 1972a).

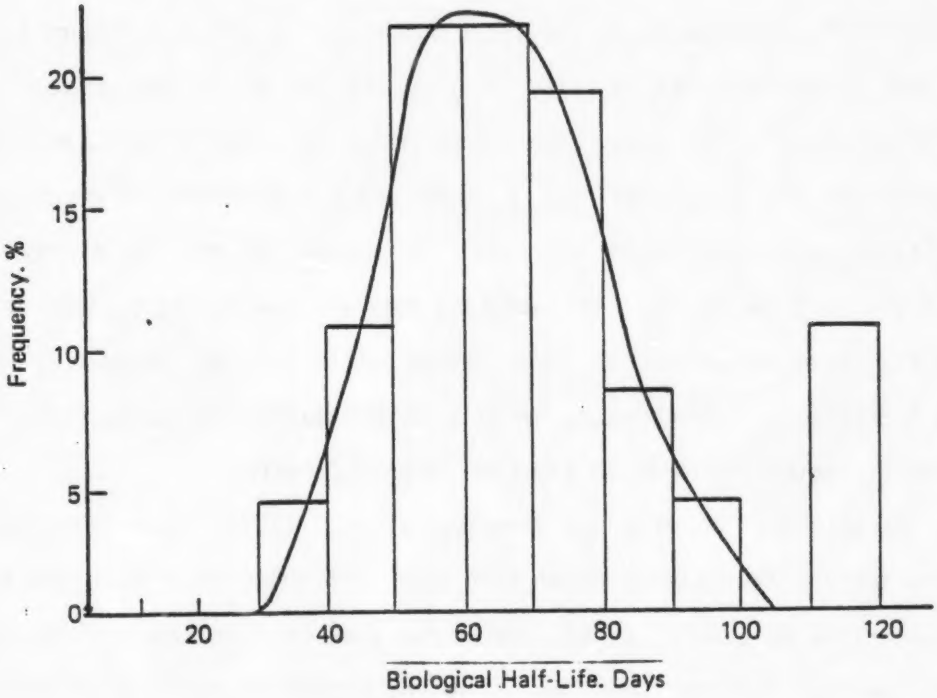

FIGURE 6

Population distribution curve of methylmercury

Source: Shahristani and Shihab, 1974

EFFECTS

Greatest emphasis will be placed on those effects occurring at the lowest levels of exposure to mercury and to the target systems that suffer effects most hazardous to the animal at the lowest exposure. Greater weight will be given to human data when reliable; otherwise, animal data will be used.

This section gives separate treatment to the physical and chemical forms of mercury that are toxicologically distinct. The short-chain alkyl mercurials, mercury in the zero oxidation state (mercury vapor and liquid metallic mercury) and the compounds of divalent inorganic mercury (Hg^{++}) will receive the most attention as these are the forms of mercury to which man is most frequently exposed.

Acute, Subacute, and Chronic Toxicity

Methylmercury and Other Short-Chain Alkyl Mercurials: The toxic effects of methylmercury have been described in several recent reviews (Swedish Expert Group, 1971; Norton, 1971; WHO, 1972, 1976; Miller and Clarkson, 1973; Friberg and Vostal, 1972; Nordberg, 1976; NAS, 1978). A major conclusion of these reviews is that prenatal methylmercury poisoning differs qualitatively and probably quantitatively from postnatal poisoning. These two situations will be treated separately in this section.

Effects on Adults: Prior to the major outbreaks in Japan in the 1950s and 1960s, cases of poisoning due to occupational and accidental methylmercury exposure had already indicated the principal signs and symptoms of severe poisoning. The first recorded poisoning took place in 1863 (Edwards, 1865). In that year, three young laboratory workers developed neurological symptoms 3 months after they were first exposed; two of them died. Four cases of methylmercury poisoning were described by Hunter, et al. (1940).

The patients had worked in a factory that manufactured methylmercury compounds for use as a seed grain fungicide. They were asymptomatic during the initial 3 to 4 months of exposure and then contracted symptoms that were confined to the nervous system. The presenting symptoms were paresthesia of the extremities, impaired peripheral field of vision, slurred speech, and unsteadiness of gait and of limbs. Examination showed that all four had ataxia, constriction of visual fields, and impaired stereognosis, two-point discrimination, and joint position sensation in the fingers. Three had dysarthria. In all cases, the maximum severity of symptoms occurred several weeks after exposure to the poison had ceased. The degree of improvement varied, and persisting neurological signs were found in all four cases. Twelve coworkers remained asymptomatic. One of the patients died in 1952 and the neuropathological findings were reported by Hunter and Russell (1954). These authors correlated the ataxia with cerebellar atrophy that particularly affected the granule cell layer, and related the visual signs to focal atrophy of the calcarine cortex.

In 1956, four patients were admitted to the hospital attached to a factory in Minamata, Japan exhibiting a neurological disorder of unknown etiology. Within a few weeks about 30 individuals with similar complaints were identified in the Minamata area. Faculty from Kumamoto University carried out investigations and by 1959 it became clear that Minamata disease was the Hunter-Russell syndrome of methylmercury poisoning (Katsuna, 1968), which resulted from the consumption of fish from Minamata Bay that were contaminated by methylmercury. The latter was discharged into the bay via the local factory effluent, but may also have been produced by biomethylation of Hg^{++} released from the factory. The hair and brain of victims contained elevated concentrations of methylmercury. Similar cases appeared in

Niigata, Japan in 1965 (Tsubaki and Irukayama, 1977). The total number of Japanese cases was recently reported to be at least 1,224 (Tsubaki and Irukayama, 1977). A poison that had previously been recognized as an occupational hazard had become identified as an environmental risk to public health.

In the late 1960s a Swedish Expert Group (1971) conducted an exhaustive review of toxicological and epidemiological data related to methylmercury poisoning in man and animals. This review was initiated as a result of the discovery that widespread mercury pollution existed in Swedish lakes and rivers, that all forms of mercury were subject to biomethylation by microorganisms present in sediments in both fresh and oceanic water, and that fish readily accumulated and concentrated methylmercury in their edible tissues. The main purpose of the group was to assess the margin of safety in the Swedish population with respect to dietary intake and risk of poisoning from methylmercury in fish. Their strategy was to obtain information on two relationships: (1) the relationship between blood concentrations and risk of poisoning (frequency of signs and symptoms) from methylmercury and (2) the relationship between long-term dietary intake and steady-state blood concentrations. By combining these two relationships they obtained estimates of risks to various groups in the Swedish populations classified according to their fish consumption. Ultimately this information was used by the Swedish government to set regulations on maximal permissible concentration of methylmercury in fish.

For information on blood concentrations and health effects, the Swedish group had to rely on limited data from the Niigata outbreak. Blood samples had been collected from only 17 patients (Figure 7); these data were insufficient to establish a statistical relationship between blood concentration and frequency of cases of poisoning (blood concentration-response). Consequently, they attempted to identify the lowest blood concentration associ-

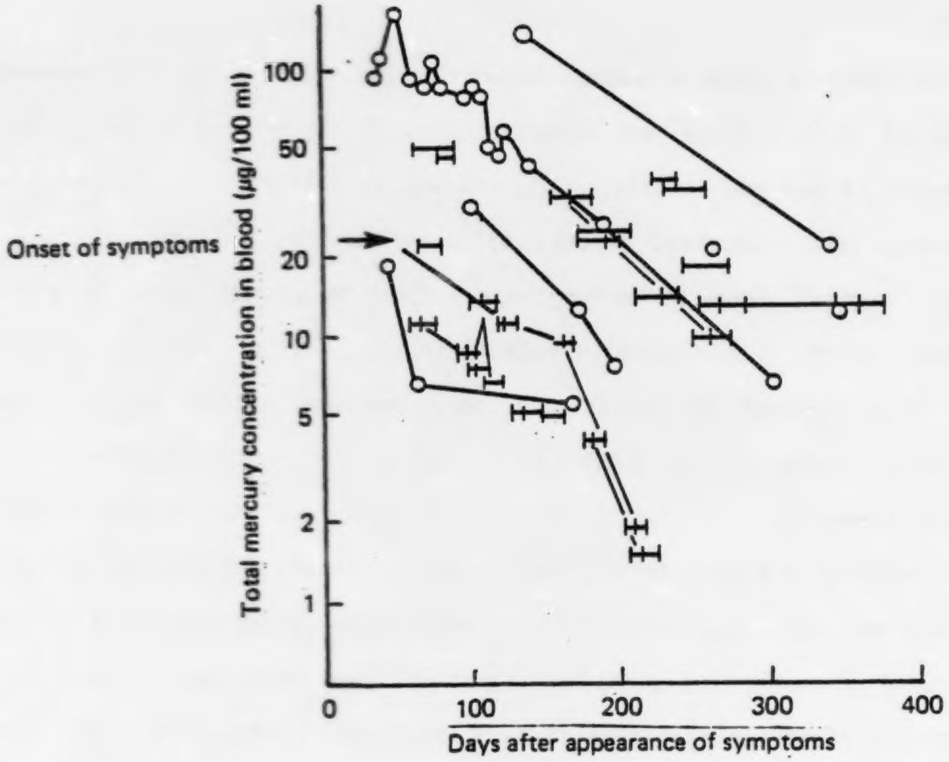

FIGURE 7.

Concentration of mercury in samples of blood collected from patients suffering from methylmercury poisoning in the Niigata outbreak. Samples from the same patients are connected by a straight line. The arrow indicates the estimated time of onset of symptoms. The units of mercury concentration in blood are µg Hg/100 ml. The numbers on the ordinate should be multiplied by ten to convert to ng Hg/ml.

Source: Swedish Expert Group, 1971.

ated with the onset of signs and symptoms of poisoning. In patients from whom several blood samples had been collected, the methylmercury concentration fell exponentially with time, corresponsing to a halftime roughly in the range of 70 days. Where sufficient data points were available, the blood concentration was extrapolated back to the time of onset of symptoms. The group concluded that the lowest concentration in blood associated with the onset of symptoms in the most sensitive individual was 200 ng Hg/ml whole blood. They calculated the maximum safe blood concentration to be 20 ng Hg/ml, using a safety factor of 10. The safety factor took into account, among other things, the greater sensitivity of the fetus as compared to adults (see Effects of Prenatal Exposure).

Information on the relationship between average daily intake and steady-state blood concentration came from two sources: radioactive tracer experiments using volunteers and dietary studies on individuals eating fish over long periods of time. Information was available on three volunteers who received an oral dose of radioactive methylmercury (Aberg, et al. (1969). Gastrointestinal absorption was virtually complete (about 95 percent of the dose) and the whole body halftime was about 70 days, roughly in agreement with the halftimes observed in blood in the Japanese patients.

Mathematical models of accumulation of methylmercury in man have been discussed previously. The accumulated amount in the body, A, would be related to the average daily amount taken up by the body, a, by the expression:

$$A = (a/b)\ (1 - e^{-bt}) \ldots\ldots\ldots\ldots (1),$$

where t is the time of exposure and b is the elimination constant, which is related to the whole body halftime T, by the expression:

$$T = \frac{\ln 2}{b} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2).$$

Equation (1) is depicted diagrammatically in Figure 5. The steady state body burden, A_{oc}, would be closely attained after exposure for a period of time equivalent to five halftimes. A_{oc} would be given by:

$$A = a/b \text{..............................} (3).$$

The tracer experiments indicated two important criteria that might be applied to dietary studies on steady-state relationship: (1) individuals should be receiving a steady daily intake for about 1 year, and (2) the accumulated amount in the body A should be linearly related to the average daily intake (equation 3). If the blood compartment equilibrates relatively rapidly with other compartments, steady-state blood concentrations should also be proportional to daily intake.

Dietary studies were conducted with Swedish fishermen and their families whose regular diet contained fish. Blood concentrations were compared to the average estimated dietary intake of methylmercury. The latter was estimated from measurements of mercury in the fish muscle and the results of careful questioning about dietary intake of fish. The results of two studies are given in Figure 8. Both studies appear to confirm a linear relationship but the slopes of the lines differ greatly. Despite the fact that the regression line of the Birke, et al. (1967) study depended heavily on one high data point, the authors rejected the other data on the basis of inaccurate dietary information. They concluded that an average daily intake of 300 μg Hg as methylmercury would yield a steady-state blood concentration of 200 ng Hg/ml and that the maximum safe daily intake would be 30 μg Hg. These conclusions were endorsed by the World Health Organization (1972) which recommended a tolerable weekly intake arithmetically equivalent to the Swedish maximum safe daily intake.

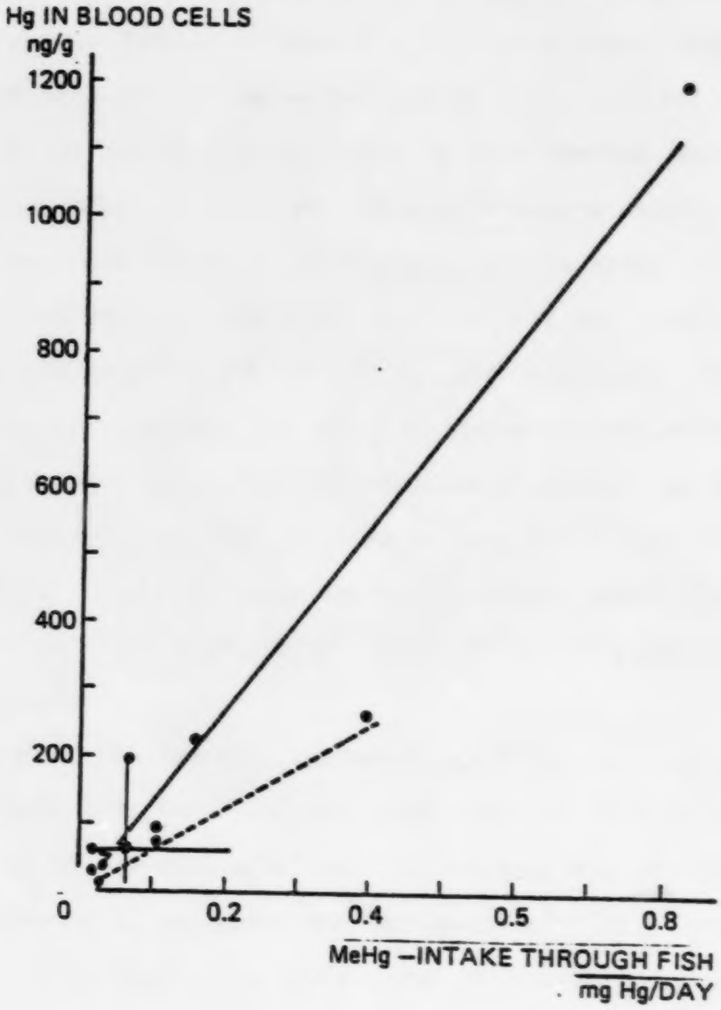

FIGURE 8.

Relation between total mercury concentrations in blood cells and exposure to methylmercury through fish. The figures in the ordinate should be divided by two to convert the concentration units to ng Hg/ml whole blood.

Source: Swedish Expert Group, 1971.

Despite the excellence of these in-depth reviews, the conclusions were necessarily limited by the quality of the data available at that time. In fact, the Swedish Expert Group (1971) pointed to several weaknesses and uncertainties in the data. (1) No information was available on the accuracy of the analytical methods used to detect mercury during the Niigata outbreak. The dithizone procedure used for the blood and hair analyses has a low sensitivity. Large volumes of blood (up to 50 ml) must have been used. In several patients, the hair to blood ratio departed from what is now believed to be the true ratio (WHO, 1976). (2) The patients were admitted to the hospital after the appearance of signs and symptoms. It was necessary to extrapolate the observed blood concentrations (based on samples collected in the hospital) back to the time of onset of symptoms. The statistical uncertainty in the linear regression extrapolation was high. (3) The Swedish data relating dietary intake to blood concentration are also fraught with uncertainty.

By the time more recent major reviews appeared (Nordberg 1976; WHO, 1976), several studies had been published on fish-eating populations and preliminary reports had appeared on the large outbreak of poisoning in Iraq. Miettinen (1973) had completed his study on 14 volunteers taking radioactive methylmercury. His data, along with observations of exposed populations in Iraq and elsewhere, allowed development of a compartmental model for uptake, distribution, and excretion of methylmercury in man (see Pharmacokinetics section). The World Health Organization review adopted a similar approach as the Swedish Expert Group in defining relationships: (1) between symptoms and blood concentration, and (2) between daily intake and steady-state blood concentrations.

A World Health Organization Committee examined the Iraqi data on adults (WHO, 1976). The outbreak in Iraq occurred in the winter of 1971-1972 among people living in rural areas. These people consumed homemade bread prepared from seed grain that had been treated with a methylmercury fungicide. There were 459 deaths among 6,540 hospitalized cases; many others were not admitted to the hospitals (Bakir, et al. 1973). Cases of severe poisoning and fatalities that occurred outside of hospitals may have been considerably greater. The Iraqi data derive from three studies: (1) a preliminary report based on 120 patients (Bakir, et al. 1973); (2) an epidemiological survey by a WHO team involving 956 persons in a heavily affected rural village and 1,014 persons in a control village (Mufti, et al. 1976); and (3) an Iraqi study by Shahristani, et al. (1976) of 184 persons in rural areas, 143 of whom consumed the contaminated bread.

Using the data of Bakir, et al. (1973), Clarkson, et al. (1976) compared the frequency of paresthesia with mercury concentrations in blood (Figure 9). Frequencies of paresthesia (5 to 10 percent) observed at low Hg concentrations were interpreted to be background values for the population and unrelated to methylmercury. The point of intersection of the two lines representing paresthesia frequencies and Hg concentrations was taken to indicate the blood Hg concentration at which paresthesias due to methylmercury emerge above the background frequency. This blood Hg concentration is 290 ng Hg/ml. However, the Hg concentrations were those existing 65 days after cessation of exposure to methylmercury and, in view of the reported blood Hg halftimes of 65 days in these patients, the maximum blood Hg concentration was probably about 480 ng Hg/ml whole blood at the end of exposure.

The Shahristani, et al. (1976) study reported no cases of methylmercury poisoning occurring below a hair concentration of 120 µg Hg/gm hair, equivalent to about 480 ng Hg/ml whole blood. The World Health Organization study

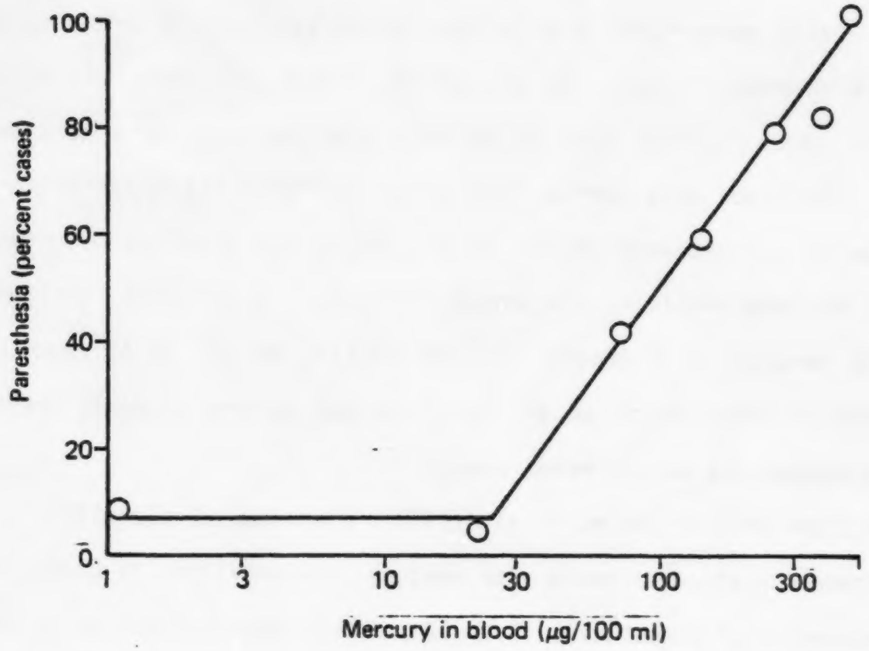

FIGURE 9.

The frequency of paresthesia as a function of the concentration of mercury in blood 65 days after cessation of exposure. The graph uses data from Table 4 of Bakir, et al. (1973). The mean blood concentrations are computed as the logarithmic means for each cohort in their table. The line connecting the first two points was assumed to be horizontal. The line connecting the other points was computed by least squares linear regression analysis

Source: Clarkson, et al. 1976.

(Mufti, et al. 1976) measured total dose according to the amount of contaminated bread consumed. The relationship between frequency of paresthesia and total dose of methylmercury had the same general relationship as that shown in Figure 9. The background parasthesia frequency was estimated to be about four percent (WHO, 1976), and the total body burden of methylmercury at which paresthesias due to methylmercury emerged above the background frequency was approximately 37 mg. Since the average body weight in the group was 50 kg, this dose would correspond to 50 mg in a 70 kg human. The equivalent blood concentration would be approximately 500 ng Hg/ml whole blood.

The Iraqi studies failed to identify a diagnosed case of methylmercury poisoning at 200 ng Hg/ml whole blood. If such cases existed, they could not be differentiated from individuals having nonspecific signs and symptoms. The Iraqi studies clearly show a need for more specific tests for effects of methylmercury at low doses.

Several studies of fish-eating populations were also reviewed by the World Health Organization (1976). Findings in Peru (Turner, et al. 1974) and Samoa (Marsh, et al. 1977) agreed with those from other fish-eating populations. No adverse health effects in adults could be associated with exposure to methylmercury from fish. However, only about 15 people had blood levels in the range of 200 to 400 ng Hg/ml.

As noted previously, a wide individual variation exists in blood halftimes. A study by Shahristani and Shihab (1974) indicates a bimodal distribution in 48 Iraqis. One group, accounting for 89 percent of the samples, had a mean halftime value of 65 days, while the other group had a mean value of 119 days.

The significance of individual variation in halftimes is demonstrated by the report of Nordberg and Strangert (1976). The steady-state blood concentration for any given dietary intake of methylmercury is directly related to the biological halftime (see equations 2 and 3). These authors realized that the bimodal distribution of halftimes reported by Shahristani and Shihab (1974) predicted that a subgroup of the population (the group with the 119-day average halftime) would attain steady-state blood concentrations almost double those of the group having the 65-day halftime. Nordberg and Strangert (1976) went on to calculate the overall risk of poisoning from dietary methylmercury by combining the relationships of the blood concentration versus frequency of paresthesia (reported by Bakir, et al. 1973) with the bimodal distribution of halftimes. A result of their calculation is given in Figure 10.

Since the WHO review (WHO, 1976) some reports had appeared on Canadian Indians exposed to methylmercury in fish. Residents of two Ojibway Indian Reserves in Northwestern Ontario had blood levels of total mercury from 5 to 330 ng Hg/ml most of which was in the form of methylmercury (Clarkson, et al. 1975). A Japanese team conducted clinical examinations on 89 residents of the two reserves out of a total population of about 1,200 (Harada, et al. 1976). A variety of sensory, coordination, and other neurological disturbances were found (paresthesia, visual field constriction, ataxia, dysarthria) similar to those reported in cases of methylmercury poisoning in Japan. However, as the authors pointed out, the neurological symptoms were relatively mild and many were thought to be due to other causes.

A Canadian medical team examined 49 Cree Indians living in northwestern Quebec and exposed to methylmercury in fish. They concluded that at least 6 and possibly 25 had signs and symptoms of methylmercury intoxication (Barbeau et al. 1976). The blood levels of mercury were elevated, 80 percent having levels above 50 ng Hg/ml.

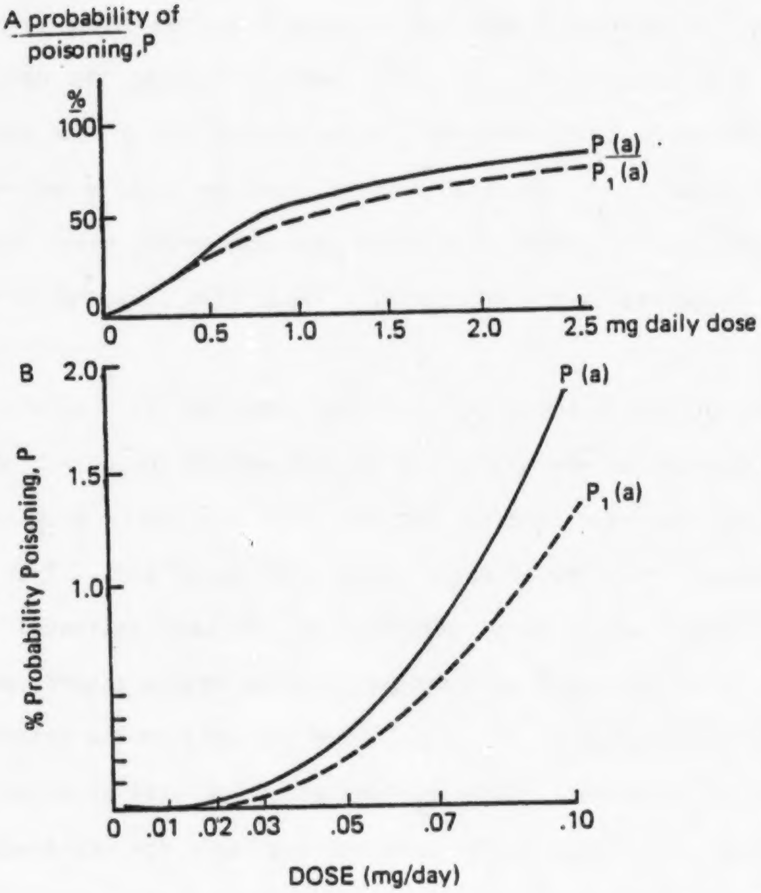

FIGURE 10.

Dose-response curve for long-term exposure to methylmercuric compounds in human beings (50 kg body wt). A, whole dose-response curve; B, detailed presentation of the curve representing lower doses. a, daily dose of Hg in the form of $MeHg^+$; P(a), probability of poisoning calculated for the total population; $P_1(a)$, probability of poisoning for the part of the population with biological halftime of 64 days. Probability P = 1.0 corresponds to 100 percent.

Source: Nordberg and Strangert, 1976.

The lack of appropriate controls for such confounding factors as age, alcohol intake, and nutrition, make it impossible to draw conclusions on the role of methylmercury in the clinical picture of both the Harada and Barbeau investigations. A National Academy of Science Committee (NAS, 1978) in reviewing data available to the WHO group (WHO, 1976) and the Canadian reports, concluded that "Until more definitive evaluations of the exposed native Canadian populations and the prenatal and perinatally exposed Iraqi populations have been completed, the guidelines concerning human exposure to methylmercury suggested in the WHO document (WHO, 1976), ...should be adhered to."

New data on the Niigata outbreak was reported by Tsubaki, et al. (1978). He reported on new analytical determinations by atomic absorption method of mercury in hair samples that had been previously analyzed by the dithizone method at the time of the Niigata outbreak in 1965. They reported that in one patient whose hair concentration had been estimated to be 52 μg/g at the time of the onset of symptoms, the new atomic absorption analyses indicated a value of about 82 μg/g. Other patients in the original Niigata group had estimated hair concentrations about 100 μg/g at onset of symptoms. Unfortunately, blood samples were not available for reanalysis by the atomic absorption procedure. In the original group of patients, (Figure 7; Swedish Expert Group, 1971), one patient had an estimated blood concentration at the time of onset of symptoms of approximately 200 ng Hg/ml. However, the extrapolation had to be made with only three data points. Furthermore, the concentration of mercury in the hair sample taken from the same patient indicated that the corresponding blood concentration should have been higher. All other blood samples in the original group in Figure 7 when extrapolated back to time of onset of symptoms, yielded values above 300 ng Hg/ml. These new data would suggest that previous evaluations of the original data from Niigata had overestimated the risk and that evidence for a lowest observable effect level (LOEL) of 200 ng Hg/ml blood had been weakened.

In the same publication, Tsubaki reported on clinical followup studies of four patients who were exposed to methylmercury in the Niigata outbreak. These patients developed symptoms of methylmercury poisoning several years after the original outbreak. The maximum hair concentrations in the four patients were between 50 and 300 μg/g as measured by atomic absorption. They were described as "methylmercury poisoned patients with delayed onset." The patients had mild nonspecific symptoms so that methylmercury poisoning could not be diagnosed with certainty. However, the Tsubaki, et al. report on delayed onset of symptoms is supported by observations on nonhuman primates. Evans, et al. (1977) reported that the length of the latent period in monkeys was inversely related to the steady-state blood concentrations. Latent periods of up to 1 year were found at the lowest doses.

In brief, analytical data from Japan points to an overestimate of risk by previous evaluation (Swedish Expert Group, 1971).* The clinical followup indicated that delayed cases of poisoning may be associated with hair concentrations as low as 50 μg/g. This evidence as well as the animal data from Evans, et al. (1977), and the continuing studies on Canadian Indians, indicate that it would be prudent to retain 200 ng Hg/ml as the lowest observable effect level in nonpregnant adults.

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*However, it should be noted that dithizone and atomic absorption methods disagreed only in the one patient who had the lowest hair concentration. Agreement was excellent between the two methods in hair samples from two other patients. Agreement between the two methods was found at mercury concentrations below 50 μg/g.

Several important conclusions may be drawn from these studies of adult poisonings. (1) More data are needed on the prevalence of effects at the lower regions of the dose-response relationships. (2) More people should be studied in fish-eating populations to identify individuals having blood concentrations in excess of 200 ng Hg/ml. Even negative results would be most helpful in setting the upper limits of risk, assuming that selection processes can be eliminated. (3) Objective methods are needed to detect the first effects of methylmercury exposure. Paresthesia and other subjective complaints are the first effects associated with methylmercury poisoning, but are not good for detecting these first effects because of the high background, i.e., high frequency in nonexposed individuals. At present, no biochemical, neurophysiological, or other objective test serves as an early warning sign (Nordberg, 1976). (4) The bimodal distribution of halftimes reported by Shahristani and Shihab (1974) needs confirmation and further refining through observation of larger numbers of people. (5) Further data are needed on the relationship between long-term dietary intake and steady-state blood concentrations in order to test the model for both long and short halftime groups. The tentative blood-level limits based on the data from Iraq also need verification in another population because dietary or genetic factors may be important.

A statistical relationship has been suggested by Skerfving, et al. (1974) between frequency of chromosomal aberrations and blood concentration of methylmercury. This report was based on 37 people exposed to methylmercury through intake of various amounts of fish. The highest exposure group had blood concentrations in the range of 14 to 116 ng Hg/ml, and the nonexposed group showed concentrations in the range of 3 to 18 ng Hg/ml. However, a study made a few months after the outbreak in Iraq could find no correlation between chromosomal damage and exposure to methylmercury (Farman, 1974).

Bakir, et al. (1973) found few clinical effects associated with damage to nonnervous tissue in the victims of methylmercury poisoning. An earlier outbreak of methylmercury poisoning revealed cardiovascular effects due to renal and cardiac damage (Jalili and Abbasi, 1961).

The Swedish Expert Group (1971) reviewed case reports of dermatitis due to occupational skin contact with alkyl mercurials used as fungicides. Jalili and Abbasi (1961) and Damluji, et al. (1976) have reported exfoliative dermatitis resulting from oral ingestion of methyl- and ethylmercury compounds.

Effects of Prenatal Exposure: The earliest mention in the literature of psychomotor retardation caused by fetal exposure to methylmercury was by Engleson and Herner (1952). A Swedish family had eaten porridge made from methylmercury-treated grain. The asymptomatic mother gave birth to a daughter who appeared to be normal at birth and in the first 2 months of life. It later became clear that the child was mentally and physically retarded. Upon further examination a year or two later, she continued to have marked psychomotor retardation, and the authors (Engelson and Herner, 1952) postulated that "mercury intoxication, perhaps during early fetal life, seems to us to be a possible cause." Her father and brother were diagnosed as having mercury poisoning. Urinary mercury concentrations were elevated in the mother; no blood or hair analyses were performed.

Harada (1968) reported on 22 children from Minamata, Japan who had severe psychomotor retardation which he concluded was due to fetal methylmercury poisoning. All children came from families in which at least one other member had been diagnosed as having methylmercury poisoning, with fatal results in 13 families. Five of the mothers had experienced transient paresthesia during pregnancy but had been well otherwise. The childrens' ages ranged from 1 to 6 years at the time of initial examination and at those ages it was not possible to determine their degree of exposure to methylmercury in utero. Two of these children died and neuropathological studies were reported by Takeuchi (1968). He concluded that there was evidence of a disturbed brain development and that the cerebral and cerebellar lesions were the same as those found in kittens that had been exposed to methylmercury in utero.

In August 1969 a family in New Mexico began to eat pork from a hog that had been fed methylmercury-treated seed grain (Snyder 1971; Pierce, et al. 1972). At that time the mother was 3 months pregnant and ate the contaminated pork regularly for the following 3 months. She remained asymtomatic but delivered a severely brain-damaged infant who, at 8 months of age, was blind and hypotonic. Some other members of the family suffered severe methylmercury poisoning. This was the first report of methylmercury toxicity from eating contaminated meat and the only published fetal case in the United States (Snyder, 1971).

The Iraqi outbreak offered an excellent opportunity to develop quantitative information with regard to prenatal exposures to methylmercury. Large numbers of people, of both sexes, were exposed to a wide range of dietary intake of methylmercury within a period of a few months. Thus, pregnant females could have been exposed to a pulsed dose of methylmercury at any time during pregnancy, and might have consumed a very wide range of doses. Early studies on 15 mother-infant pairs identified infants who were prenatally exposed to and severely poisoned by methylmercury (Amin-Zaki, et al. 1974a). Choi, et al. (1977) reported abnormal neuronal migration in a human infant prenatally poisoned with methylmercury in Iraq. A group of infants was also identified that had been exposed to methylmercury primarily by sucking (Amin-Zaki, et al. 1974b).

Follow-up neurological and pediatric studies by a University of Rochester team obtained dose-effect relationships between prenatal exposure and effects on the infants (Marsh, et al. 1977). Ten infants of mothers who had maximum hair concentrations in the range of 99 to 384 ppm (µg/g) differed from two groups having lower maternal hair concentrations (12 to 85 ppm and 0 to 11 ppm, Figure 11) in the frequency of signs and symptoms of psychomotor retardation. Statistically significant differences were found ($P < .03$) by the Chi-Square test in the delayed achievement in developmental milestones (delayed walking and talking) and in the histories of seizures. The high mercury group also differed from the other two groups in the number of infants having multiple signs and of poisoning symptoms (Table 14). For example, all the infants in the high exposure group except two had three or more adverse health effects per infant. In contrast, the two groups with lower exposures consisted mainly of infants having one or no adverse effects. A statistical analysis revealed a highly significant ($P<0.005$, chi square test) difference in distribution between the high exposure and the two lower exposure groups.

The small number of infant-mother pairs in this study does not allow us to identify a specific threshold maternal hair concentration below which adverse effects do not occur in both mother and infant. A high risk of adverse effects appear to exist at maternal hair concentrations in the range of 99 to 384 ppm. However, in the next lower concentration range (12 to 85 ppm) the frequencies have fallen dramatically and do not differ significantly from those seen in the lowest range (0.5 to 11 ppm). Thus, the adverse effects seen at maternal hair concentrations up to 85 ppm may have been due to causes other than methylmercury exposure. Unfortunately, only four infant-mother pairs were available between 25 and 50 ppm maximum maternal hair concentration.

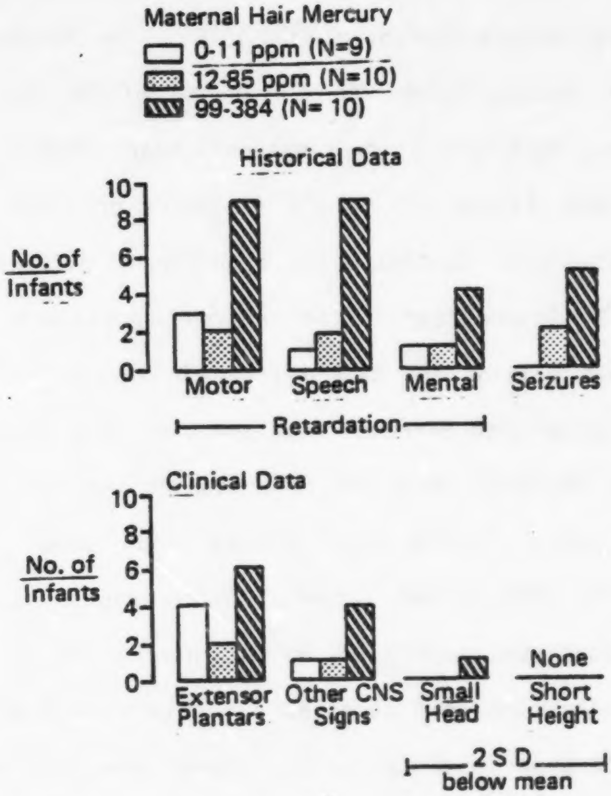

FIGURE 11.

Signs (clinical data) and symptoms of psychomotor retardation in 29 Iraqi infants exposed prenatally to methylmercury. The frequency of abnormalities are compared in groups of infants according to the maximum maternal hair concentration during pregnancy.

The following criteria for abnormalities were adopted: motor retardation if the child was not walking at 18 months, speech retardation if not talking by 24 months, mental retardation or seizures (or convulsive-like attacks) according to the history provided by the mother, and neurological signs by agreement of the two examiners. No standards are available for head circumference or height of Iraqi children, so these factors were evaluated in terms of standard deviations below the mean for the group.

Source: Marsh, et al. 1980.

Table 14

Frequency of Infants' Symptoms and Signs Related to Maternal Hair Mercury Concentration*

	No. of Infants							
Maternal Hg (ppm)	Abnormalities per Infant							Total Infants
	0	1	2	3	4	5	6	
0–11	3	5	0	0	0	1	0	9
12–85	4	4	0	2	0	0	0	10
99–384	1	0	1	2	3	1	2	10

*Source: Marsh, et al. 1980.

An epidemiological study of school children living in the Minamata area of Japan has recently been reported (Med. Tribune, 1978). Children suspected of prenatal and early postnatal methylmercury exposures (age group 8 to 16) exhibited a higher incidence of neurological deficits, learning difficulties, and poor performance on intelligence tests than children of similar age in a control area. These findings confirm predictions from studies of animals prenatally exposed to methylmercury (Spyker, et al. 1972), in which a variety of behavioral and neurological tests revealed deficits only after the animals had reached maturity.

In summary, our knowledge is still limited in perhaps the most critical area of methylmercury toxicity in man. A study on a fish-eating population is needed to complement the Iraqi program to test if methylmercury ingested from contaminated bread is equivalent toxicologically to methylmercury chronically ingested from fish. The ongoing Iraqi study has demonstrated the feasibility of relating the dose of the mother during pregnancy to effects seen in the infant during the first 6 years of life. Other effects may manifest themselves in later years as the child matures.

Effects on Animals: Animal studies reveal that effects on nonhuman primates are similar to those on man (Berlin, et al. 1973). Neurological damage has also been reported in various other species (Swedish Expert Group, 1971; WHO, 1976). In general, effects manifest themselves at the same brain concentrations but corresponding blood concentrations may differ widely due to species differences in blood to brain ratios (Figure 12).

The rat appears to experience effects not seen in man. Kidney damage has been reported by several investigators (Klein, et al. 1972, 1973; Fowler, 1972; Magos and Butler, 1972). Damage to the peripheral nervous system has been reported in rats (Somjen, et al. 1973a,b; Chang and Hartman,

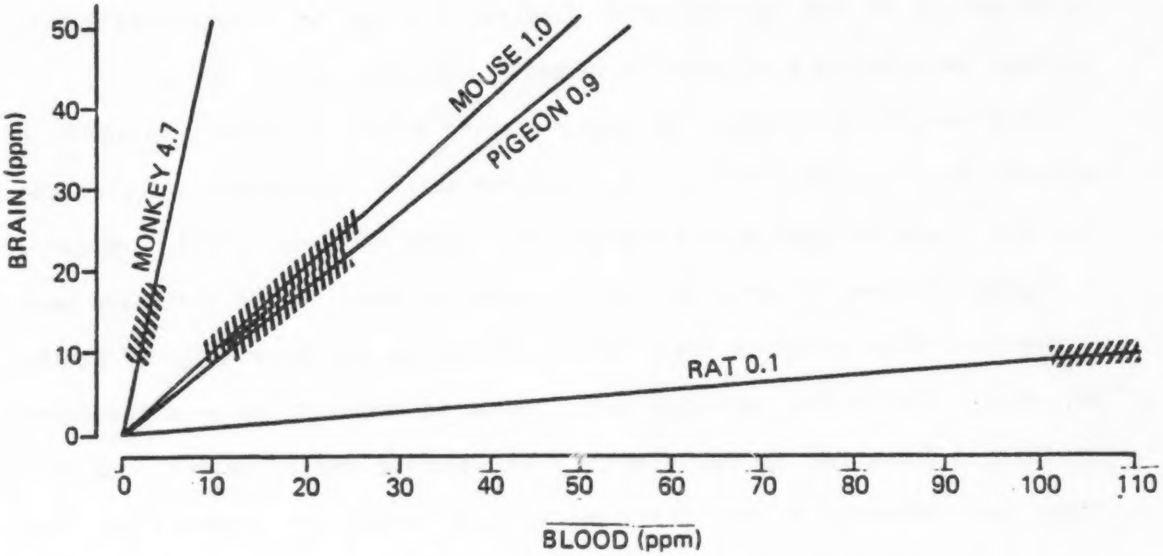

FIGURE 12.

Comprehensive brain/whole blood regression lines in four species orally dosed with methylmercury. The shaded areas correspond to the onset of the first detectable signs and symptoms of poisoning.

Source: Weiss, et al. 1978.

1972a,b), whereas neurological signs in man appear to be due mainly to damage to the central nervous system (Von Burg and Rustam, 1974). However, effects on the neuromuscular junction have been found in severe cases of poisoning in Iraq (Von Burg and Landry, 1976).

The first effects of methylmercury as evidenced by animal experiments are on protein synthesis in neurons (Yoshino, et al. 1966; Cavanagh and Chen, 1971; Chang and Hartman, 1972a, b; Syversen, 1977). The effects of methylmercury on the neuromuscular junction are due to a highly selective interaction with the acetylcholine receptor (Shamboo, et al. 1976).

Ganther, et al. (1972) reported a sparing effect of dietary selenium on methylmercury toxicity in rats and Japanese quail. Subsequent animal studies have confirmed Ganther's findings (WHO, 1976; Nordberg, 1976). However, the concentrations of methylmercury or selenium added to the diet have been higher than those found in human diets. Following the observation of Ganther, et al. (1972) that selenium salts, added to the diet, delayed the onset of toxic effects due to methylmercury in Japanese quail, several publications have appeared in the literature on selenium-mercury interactions (for review, see WHO, 1976; Nordberg, 1976). However, in the most recent evaluation of experimental data, it was concluded that there is insufficient evidence that selenium in the human diet would protect against the toxic effects of methylmercury (Permanent Comm. Int. Assoc. Occup. Health, 1977).

Effects on Adults of Mercury Vapor and Liquid Metallic Mercury: The effects of inhaled mercury vapor on human health have been known since ancient times. Recently, several reviews have dealt with this topic (Friberg and Vostal, 1972; NIOSH, 1973; Friberg and Nordberg, 1973; Nordberg, 1976; WHO, 1976). However, health effects have not been associated with oral ingestion of liquid metallic mercury.

Exposure to extremely high concentrations of mercury vapor (greater than 1 mg Hg/m^3) can damage lung tissue, causing acute mercurial pneumonitis (Milne, et al. 1970). Exposure to lower levels results in signs and symptoms indicating effects primarily on the central nervous system.

Most of our knowledge derives from studies of occupational exposures. These reviews listed above refer to observations of more than 1,000 individuals and indicate that the classical signs and symptoms of mercury vapor poisoning (mental disturbances, objective tremors, and gingivitis) occur in workers following chronic exposures to average air concentrations above 0.1 to 0.2 mg Hg/m^3 (Neal, et al. 1937, 1941; Bidstrup, et al. 1951; Friberg, 1951; Rentos and Seligmann, 1968).

In a comparative study of over 500 workers, Smith, et al. (1970) reported effects on the nervous system that were related to the time-weighted average air concentration of mercury. Objective tremors were found at air concentrations above 0.1 mg Hg/m^3. Nonspecific symptoms such as loss of appetite, weight loss, and shyness seem to occur at a greater frequency than in the control group at average air concentrations in the range of 0.06 to 0.1 mg Hg/m^3.

Extensive Russian studies on occupationally exposed workers have been reported in a monograph by Trachtenberg (1969) and reviewed by Friberg and Nordberg (1973). A syndrome involving insomnia, sweating, and emotional lability was claimed to occur at a higher frequency as compared to controls in workers exposed at high ambient temperatures (40 to 42°C in summer and 28 to 38°C in winter) to mercury concentrations in the range of 0.006 to 0.1 mg Hg/m^3.

Considerable uncertainty still exists with regard to health effects at concentrations below 0.1 mg Hg/m^3. Friberg and Nordberg (1973) point to the possibility of "interviewer" effects in occupational studies in which the factory physician is aware of the mercury concentration to which the workers are exposed.

In the study of Trachtenberg (1969), uptake of iodine by the thyroid was significantly greater in a mercury-exposed group of workers than in a control group. However, Kazantzis (1973) has suggested that these studies should be repeated and should include measurements of serum thyroxin. He pointed out that increased uptake of radioactive iodine will occur if the store of iodine in the thyroid gland is low and need not necessarily be associated with increased secretion of thyroxin.

Four cases of proteinuria were reported in workmen exposed to mercury vapor (Kazantzis, et al. 1962). Exposure levels were probably high, as urinary concentration was in excess of 1,000 µg Hg/l. Increased urinary excretion of protein in exposed versus nonexposed workers was reported by Joselow and Goldwater (1967). Ashe, et al. (1953) found morphological evidence of kidney damage in rabbits exposed to mercury vapor.

Few biochemical changes have been reported due to inhalation of mercury vapor. Wada, et al, (1969) noted that blood cholinesterase activity was decreased when urinary mercury excretion was greater than 200 µg Hg/g of urinary creatinine. This rate of excretion should correspond to an average air concentration slightly lower than 0.1 mg Hg/m^3 (Wada, 1969).

Table 15, which summarizes data from animal and human studies, shows that the earliest effects of mercury vapor appear at roughly similar brain concentrations in a variety of species. Because of species differences in ventilation rates and pharmacokinetics parameters of inhaled mercury, the same brain concentration in various species would not necessarily correspond to the same average air concentration.

TABLE 15

Estimated Average Brain Concentrations at which Toxic Effects Appear in Adult Humans and Animals

Species	Brain Conc. µg Hg/g wet wt.	Severity of effects	Reference
Rabbit	1.0 (approx.)	mild[a]	Ashe, et al. (1953)
Rat	2.8	mild[a]	Rothstein and Hayes (1964)
Rat	1.9	mild[a]	Berlin, et al. (1969)
Human	0.85	mild[b]	Estimated[c] from Hurch, et al. (1976) Smith, et al. (1970)

[a] The animals were described as irritable.

[b] Subjective symptoms such as complaints of loss of appetite.

[c] The steady-state brain concentration was estimated from the data of Hurch, et al. (1976), which show that 7 percent of an inhaled dose is deposited in the brain, and that the halftime in brain is 21 days. Brain weight was assumed to be 1.5 kg, and the time-weighted average air concentration associated with mild effects to be 0.1 ng Hg/m^3, according to data of Smith, et al. (1970). Workers were assumed to inhale 10 m^3 air during an 8-hour occupational exposure, to retain 80 percent of the inhaled mercury, and to work for 5 days per week.

Effects of Prenatal Exposure: Little information is available on biological effects in humans due to prenatal exposure to mercury vapor. Studies carried out early in this century suggest that women chronically exposed to mercury vapor experienced increased frequencies of menstrual disturbances and spontaneous abortions; also, a high mortality rate has been observed among infants born to women who displayed symptoms of mercury poisoning (Baranski and Szymczyk, 1973). However, the degree of exposure of these women to mercury vapor is unknown. In 1967, an epidemiological survey in Lithuania called attention to an increased incidence of abortion and mastopathy related to duration of time on the job among women working in dental offices where mercury vapor concentrations ranged up to 0.08 mg/m^3 (Baranski and Szymczyk, 1973). Another report described the case of a woman chronically intoxicated by mercury vapor in whom two pregnancies ended unfavorably. After recovering from overt mercury poisoning, this woman gave birth to a healthy child (Derobert and Tara, 1950).

In summary, little is known about the reproductive effects of inhaled mercury vapor. In view of the observed reproductive effects of other forms of mercury, studies are urgently needed in this area.

Salts of Inorganic Mercury: The lethal oral dose in man of $HgCl_2$ has been estimated to be between 1 and 4 grams (Gleason, et al. 1957). Death is due to acute renal failure. The effects of chronic exposure to salts of inorganic mercury have not been described in man. Long-term occupational exposure to $Hg(NO_3)_2$ must have occurred in the felt hat industry (Neal, et al. 1937). However, poisoning was believed to be due to inhalation of mercury vapor produced from $Hg(NO_3)_2$ during the procedure of treating the felt.

Fitzhugh, et al. (1950) treated rats with $HgCl_2$ added to the food for periods of up to 2 years. Morphological changes were induced in kidney tissue at dietary concentrations of 0.5 μg Hg/g food. However, these studies have been criticized by Goldwater (1973) who noted that no effects were produced in other groups of rats receiving much higher dietary levels of mercury (2.5 to 10 μg Hg/g).

Compounds of inorganic mercury have been shown to be diuretic in dogs (Mudge and Weiner, 1958). The nature of the anion is important. Inorganic mercury complexed with cysteine is a more potent diuretic than $HgCl_2$.

Piotrowski, et al. (1973) have discussed the role of metallothionein in controlling the toxic action of Hg^{++} on the kidney. The authors pointed out that the toxic effects on the kidney following a single dose of Hg^{++} salt appear when the metallothionein binding capacity is exceeded. Repeated daily doses of Hg^{++} cause induction of metallothionein synthesis. Consequently, much higher concentrations of inorganic mercury may be tolerated by the kidney after chronic exposures (Clarkson, 1977).

Aryl, Alkoxy-aryl, and Other Organic Compounds of Mercury: Despite the widespread usage of phenyl mercury compounds, little information is available regarding their effects on human health. Since Goldwater's review (1973), new information has come to light. No evidence of adverse health effects could be found in 67 workers occupationally exposed to phenyl mercury compounds. Air concentrations were generally below 0.1 mg Hg/m^3. Elemental vapor was the principal form of mercury in air.

A case of acrodynia has been reported in a child allegedly exposed to mercury after the bedroom had been painted with paint containing phenyl mercury compounds. The form of mercury in the air was not identified but it is likely that mercury vapor was a principal component (Hirschman, et al. 1963).

Goldwater (1973) referred to seven workers who had spent about 6 weeks working with material containing methoxyethyl mercury chloride. Remarkably high blood levels were reported (range 340 to 1,090, average 650 ng Hg/ml) 4 weeks after the end of exposure. No adverse health effects could be detected.

Rats exposed for 2 years to phenyl mercury acetate in the diet exhibited morphological changes in the kidneys (Fitzhugh, et al. 1950). As pointed out by Goldwater (1973), a dose-response relationship was not established, as animals receiving higher doses showed no effect.

Teratogenicity

Methylmercury and Other Short-Chain Alkyl Mercurials: Although brain damage due to prenatal exposure to methylmercury has occurred in human populations, no anatomical defects have been reported. However, adequate epidemiological studies have not been performed and the possibility of teratological action of methylmercury in human subjects cannot be dismissed at this time.

Embryotoxicity and teratogenicity of methylmercury in animals have been reported by several authors. Oharazawa (1968) noted an increased frequency of cleft palate in mice treated with an alkyl mercury phosphate. Fujita (1969) treated mice to daily administration of 0.1 mg Hg/kg of methylmercury and found that the offspring had significantly reduced birth weight and possible neurological damage. No gross teratological effects were noted. Histological evidence of damage to the brain as a result of prenatal exposure to methylmercury has been reported on several animal species (Matsumoto, et al. 1967; Nonaka, 1969; Morikawa, 1961). Non-lethal anatomical malformations in animals prenatally exposed to methylmercury have also been reported by Spyker and Smithburg (1972) and Olson and Massaro (1977). Effects due to prenatal exposure in mice were found to be about twice as great as those induced by postnatal exposure and were greater when the methylmercury was administered late in the period of organogenesis.

Mercury Vapor and Liquid Metallic Mercury: Although the syndrome of mercury vapor poisoning has long been known in adults, practically nothing is known about prenatal damage. Rats exposed prenatally to mercury vapor are reported to have died within 6 days after birth. In one experiment, where exposures were continued throughout gestation, all of the pups died; some of the deaths could be attributed to a failure of lactation in the dams. A second part of the experiment exposed the dams only prior to the time of impregnation. In this case, during lactation and nursing, viable pups appeared normal, yet 25 percent of these pups died before day 6. No teratological effects were observed, birth weights were reportedly within the normal range, and histopathologic findings were negative, although the concentrations of vapor were high (LC_{25} for the adult females) (Baranski and Szymczyk, 1973).

Salts of Inorganic Mercury: Teratological effects of $HgCl_2$ have been reported in animals (Gale and Ferm 1971). However, no data are available on the teratogenicity of inorganic mercury in human populations.

Mutagenicity

Methylmercury and Other Short-Chain Alkyl Mercurials: No mutagenic effects have been reported in human populations due to exposure to methylmercury. However, a statistical relationship was found between the frequency of chromosome breaks and blood concentrations of methylmercury in 23 Swedish subjects on fish diets. The mercury concentration in the blood of the exposed group ranged from 14 to 116 ng Hg/ml, and in the nonexposed group from 3 to 18 ng/ml (Skerfving, et al. 1974).

Khera (1973) has reported that, in rats, alkylmercury compounds may damage gametes prior to fertilization. Similar experiments in mice failed to demonstrate statistically significant effects (Suter, 1975). Studies by Ramel (1972) have revealed damage to reproduction resulting from exposure to alkylmercurials during adult life. Methylmercury has been shown to block mitosis in plant cells, human leukocytes treated *in vivo*, and human cells in tissue culture, and to cause chromosome breakage in plant cells and point mutations in Drosophila (Swedish Expert Group, 1971; Ramel, 1972).

Mercury Vapor and Liquid Metallic Mercury: Nothing has been reported on the mutagenic effects of mercury vapor in humans, animals, or *in vitro* tests.

Salts of Inorganic Mercury: Reversible inhibition of spermatogonial cells has been observed in mice treated with $HgCl_2$ (Lee and Dixon, 1975). No evidence has been published concerning the mutagenicity of mercury salts in humans.

Carcinogenicity

When metallic mercury was injected intraperitoneally into rats, sarcomas were observed only at those tissues that had been in direct contact with the metal (Druckrey, et al. 1957).

No other evidence exists that links exposure to mercury with cancer.

CRITERION FORMULATION

Existing Guidelines and Standards

A World Health Organization expert group has recommended an international standard for drinking water of 1 μg Hg/l (WHO, 1971); the U.S. Environmental Protection Agency has recommended a standard of 2 μg Hg/l (U.S. EPA, 1973).

Current Levels of Exposure

The median levels of total mercury for various bodies of uncontaminated water were summarized in Table 7. This information is also presented later in this document in Table 18 to allow consideration with the derived criteria values. Reported values are reviewed in the main text of this document. In general, values for uncontaminated freshwater do not exceed 200 ng Hg/l and for ocean water 125 ng Hg/l. It is likely that the wide range of reported individual values are a result of difficulties in obtaining precise analytical measurements (McLean, et al. 1980).

Measurements of different chemical and physical species of mercury in natural waters have rarely been made. It is suspected that a wide variety of different chemical compounds of mercury are present, that the relative proportions may vary from one body of water to another, and may vary seasonally. Methylmercury compounds are below the limit of detection by most methods and amount to a small fraction (probably less than 3 percent) of the total mercury. Nevertheless, this small amount of methylmercury in water probably determines uptake by fish either directly through the gills or indirectly through the food chain.

Methylmercury in edible fish is the predominant, if not the only, source of methylmercury exposure to human populations.

Special Groups at Risk

The evidence presented in this document indicates that intake of mercury from drinking water is negligible. Human exposure to the most hazardous form of this metal, methylmercury, is almost exclusively via consumption of fish. Thus, the population most likely to be at risk is heavy consumers of fish containing the highest mercury concentrations. The stage of the human life cycle subject to the greatest hazard from mercury intake is probably prenatal.

Other forms of mercury probably do not present a significant risk, except in the case of mercury vapor. The latter may present a health risk if occupational exposures are not maintained below acceptable limits. Unfortunately, the stage of the life cycle most susceptible to the toxic effects of mercury vapor has not yet been identified.

An unusual and rare reaction to inorganic mercury forms, called acrodynia or "Pink's Disease," has been described. This disease has occurred in children receiving oral doses of medications containing inorganic mercury, or inhaling mercury vapor. Only a small number of children develop acrodynia when exposed to mercury. It is unlikely that a small amount of inorganic mercury ingested in drinking water would cause this disease.

Basis and Derivation of Criterion

From a health effects perspective and recognition of exposure potential the organo-mercury compounds are the most important, especially methylmercury. However, inorganic compounds of mercury should also be considered because of their toxicity potential, and perhaps more importantly because of the ease with which inorganic mercury can be converted to organo-mercury compounds in biological systems. Methylation and demethylation are discussed in the text of the criterion document (see Exposure section conclusion).

The approach that has been adopted in this criterion document involves the following steps: (1) Identify those organs or tissues most sensitive to damage by the different chemical and physical forms of mercury. Damage being defined as an effect that adversely changes normal function or diminishes an individual's reserve capacity to deal with harmful agents or diseases. (2) Determine the lowest body burden known to be associated with functional damage in man and, if possible, determine the highest body burden tolerated by man. (3) Estimate the potential human intake from ingesting water and eating contaminated fish products. (4) Estimate a criterion for mercury in ambient water that will provide adequate protection from adverse effects on human health.

Table 16, taken from the review by the World Health Organization expert group (WHO, 1976), indicates long-term daily intakes of mercury which relate to the earliest effect on the central nervous system. This system is more sensitive to damage from mercury than other functional systems in the human body. The conclusions represented in Table 16 were recently endorsed by the National Academy of Sciences (NAS, 1978).

Evidence reviewed in the Effects section of this document is essentially the same as the evidence reviewed by the WHO group with regard to adult exposures to mercury. Effects on the adult nervous system have been estimated to occur at blood concentrations in the range of 200 to 500 ng Hg/ml, corresponding to a long-term daily intake of mercury in the diet of 3 to 7 ug Hg/kg body weight. The risk of effects at this intake level is probably less than 8 percent (1 in 12 chances).

Since the WHO (1976) criteria document was written, new evidence has been documented. As reported in the Effects section, clinical follow-up studies of the Niigata outbreak (1978) point to delayed cases of mercury

TABLE 16*

The Concentrations of Total Mercury in Indicator Media and the Equivalent Long-Term Daily Intake of Mercury as Methylmercury Associated with the Earliest Effects in the Most Sensitive Group in the Adult Population[a,b]

Concentrations in indicator media		
Blood (ng/ml)	Hair (µg/g)	Equivalent long-term daily intake (µg/kg body weight)
200-500	50-125	3-7

*Source: WHO, 1976.

[a] The risk of the earliest effects can be expected to be between 3 to 8 percent.

[b] The table should not be considered independently of the text.

poisoning. One case had a maximum hair concentration of 50 µg/g. Thus, despite conclusions based on new analytical results indicating that the lowest observed effect level had been underestimated, the new clinical data from Japan are still consistent with a LOEL of 200 ng Hg/ml in blood. New data from Iraq indicated females who experienced maximum hair concentrations during pregnancy in the range of 99 to 384 µg Hg/g had a high probability of having retarded development in children (Mufti, et al. 1976). Unfortunately, the population size was too small to establish a lower limit to effects of prenatal exposure. A hair concentration of 99 µg Hg/g is equivalent to a blood concentration of about 400 ng Hg/ml.

The most recent information on the effect of mercury on human health has come from the study of the Iraq outbreak of 1971-1972. The followup of the cases of prenatal exposure is still in progress. As noted by the National Academy of Sciences (1978), "continued careful evaluation of this very important cohort of prenatally exposed individuals will provide the most sensitive assessment of human mercury toxicity."

Thus, at this stage of knowledge of the dose-effect relationship of mercury in man, it appears that the earliest detected effects in man are at blood concentrations between 200 and 500 ng Hg/ml, for both pre- and postnatal exposures. Blood concentrations of mercury correspond to body burdens in the range of 30 to 50 mg Hg/70 kg body weight, and to long-term daily intakes in the range of 200 to 500 µg Hg/70 kg.

Mercury intake from drinking water, according to data reviewed in the Exposure section of this document, is generally less than 1 µg Hg/day, and is considerably less than the diet portion (Table 17). Assuming that the concentration of mercury in all samples of drinking water is at the current U.S. EPA standard of 2 µg Hg/l, the maximum daily intake would only be 4 µg Hg, assuming 2 liters of drinking water are consumed per person each day. This maximum intake would amount to only about 1 to 2 percent of the

TABLE 17

Estimate of Average and Maximum Daily Intakes of Mercury by the "70 kg Standard Adult" in the U.S. Population[a]

Media	Mercury intake µg/day/70 kg Average	 Maximum[b]	Predominate form
Air	0.3	0.8	Hg^0
Water	0.1	0.4	Hg^{++}
Food	3.0	5.0	CH_3Hg^+

[a] For details on the calculation of these numbers, see the Exposure section of this document.

[b] These are approximate figures indicating that 95 percent of the population have intakes less than these figures. Occupational exposures are not included.

minimum toxic intake given in Table 16. Thus, from the toxicological standpoint, exposure to mercury, via drinking water only, would be negligible.

Indirect transfer of mercury from water to man is much more important than transfer from direct routes. This conclusion is based on the assumption that fish bioaccumulate a significant amount of mercury from water. In theory, it should be possible to calculate the maximum concentration of mercury in water which would ensure that intake from fish does not exceed the lowest observable effect level (LOEL) in man. Thus, if the bioconcentration factor is known for each species of edible fish, it is arithmetically simple to estimate the maximum concentration of mercury in water.

Calculation of Criteria for Mercury in Natural Waters

BCF values have been determined experimentally in a limited number of cases. Experiments were made for both freshwater and marine fish. Inorganic and methylmercury compounds were used. The range of values for the BCF was enormous, from 250 to 60,000. Estimating a mean value from such a wide range would not be realistic. Indeed, there are both practical and theoretical difficulties in measuring an experimental BCF that is applicable to mercury accumulation by fish in natural waters. Instead, a practical BCF has been estimated based on observed average concentrations in fish and in the natural bodies of water in which the fish live (Table 18). The practical values of the BCF, referred to as PBCF, are average values covering the whole range of fish sizes, and water temperatures, averaging chemical and physical species of mercury, and other factors that may be expected to affect the fish accumulation of mercury (Table 18). The PBCFs depend upon the assumption that fish accumulation of mercury is related to the average concentration of total mercury in natural water, as discussed in detail in the main document. Specifically, uptake of mercury by a fish whether by direct

TABLE 18

Data Used in the Estimation of Average Individual Fish Intake, Average Individual Mercury Intake, Average Practical Bioconcentration Factors for Bodies of Fresh Water, Estuarine-coastal Water, and Open Oceans

SPECIES	FISH INTAKE[a]		TOTAL MERCURY[b]		
	Proportion by weight	Amount g/day	Concentration in edible tissue µg/g	Average intake µg/day/70kg	PBCF
FRESH WATER					
Trout	0.030	0.561	0.240[c]	0.135	6000
Bass	0.025	0.467	0.200[c]	0.093	5000
Catfish	0.025	0.467	0.070[c]	0.0327	1750
Pike	0.012	0.224	0.390[c]	0.0873	9750
TOTAL		1.719		0.348	
MEDIAN					5500
ESTUARINE - COASTAL WATERS					
Shrimp	0.102	1.910	0.050[c]	0.0950	2941
Flounder	0.049	0.910	0.100[c]	0.0910	5882
Clams	0.038	0.711	0.050[c]	0.0356	2941
Crabs/ Lobsters	0.037	0.692	0.090[e]	0.0623	5294
Oysters/ Scallops	0.030	0.561	0.030[c]	0.0168	1765
TOTAL		4.78		0.301	
MEDIAN					3765

TABLE 18 (continued)

Data Used in the Estimation of Average Individual Fish Intake, Average Individual Mercury Intake, Average Practical Bioconcentration Factor for Bodies of Fresh Water, Estuarine-coastal Water, and Open Oceans

OPEN OCEANS

SPECIES	FISH INTAKE[a]		TOTAL MERCURY		
	Percent total by weight	Amount g/day	Concentration in edible tissue µg/g	Average intake µg/day/70kg	PBCF
Tuna	0.214	4.00	0.205[c]	0.820	13,666
Unclassified	0.184	3.441	0.140[d]	0.4817	9,333
Ocean Perch	0.050	0.935	0.130[c]	0.1216	8,666
Salmon	0.034	0.636	0.050[c]	0.0318	3,333
Cod	0.027	0.505	0.130[c]	0.0657	8,666
Haddock	0.025	0.467	0.110[c]	0.0514	7,333
Pollock	0.020	0.374	0.14[c]	0.0524	9,333
Sardines	0.018	0.337	0.02[e]	0.0067	1,333
Halibut	0.011	0.206	0.197[e]	0.0406	13,133
Snapper	0.011	0.206	0.30[f]	0.618	20,000
Whiting	0.009	0.168	0.12[f]	0.0202	8,000
All Other	0.051	0.954	0.14[d]	0.1336	9,333
TOTAL		12.229		2.4437	
MEDIAN					9,000

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[a] Cordle, et al. 1978, Table 8, total fish intake were taken as 18.7 g/day/70 kg.

[b] Associated total Hg water concentration were 40 ng/l for fresh water; 17 ng/l for estuarine-coastal waters, and 15 ng/l for the open ocean. For details, see chapter on Exposures

[c] Table 6 of this document

[d] Mean of reported values for oceanic fish in this table

[e] Stanford Research Institute, 1975

[f] FDA, 1978

sorption in the gills or via the food chain is proportional to the average mercury concentration in natural water. It is further assumed that the methylmercury level in natural waters, on the average, is a constant fraction of total mercury.

The criterion for a natural body of water is the maximum average mercury concentration which shall not result in significant risk of adverse effects on human health from consumption of fish and drinking water. The calculation of the criterion for freshwater, shown in Table 19, was based on the assumption that 2 liters of water are consumed daily while that for estuarine-coastal and open ocean waters is based on consumption of marine or estuarine organisms only. The concentration in natural water C' that would correspond to the lowest observable effect level (LOEL) for daily human intake of mercury in the 70 kg adult is given by

$$\text{LOEL} = C' \, (2 + d \times \text{PBCF}) \, . \, . \, . \, . \, . \, (4)$$

where d (g/day/70 kg) is the average intake of freshwater, estuarine and ocean species most frequently consumed; the PBCF relates to the appropriate body of water in which the fish live.

The value of d (the daily amount of fish consumed) in equation (4) was calculated by apportioning the average total daily intake of fish from all sources—18.7 g/day—according to average individual consumption of fish from each body of natural water. Using data listed in Table 18, it was determined that the average individual fish consumption from freshwater bodies is 1.72 g/day, from estuarine-coastal waters is 4.78 g/day, and from open oceans is 12.2 g/day.

Species of fish used in the calculation are those for which information was available on human consumption and on average mercury concentration in edible tissue. The average individual mercury intake shown in Table 19 was estimated as 0.348 μg/day/70 kg individual from freshwater, 0.301 from estuarine and coastal water, and 2.44 from open ocean water.

TABLE 19

Estimation of Criteria Taking into Account Both Average Fish Consumption and Average Mercury Intake from Each Body of Water[a]

Body of water	Average individual daily consumption Fish[b] (g/day)	Mercury[b] (µg/day)	Apportioned LOEL[c] (µg/day/70 kg)	PBCF[b]	Criteria (ng/l)[d]
Freshwater	1.72	0.348	22.5	5,500	196
Estuarine Coastal	4.78	0.301	19.5	3,760	108
Open Ocean	12.22	2.44	158.0	9,000	144
Total	18.73		200.0		

[a] For details of the calculations of criteria, see text.

[b] For details, see Table 18.

[c] The lowest observable effect level (LOEL) of 200 µg/day/70 kg individual is apportioned according to the average estimated mercury intake for each body of water.

[d] Criteria concentration equals C' from equation (4) divided by a safety factor of 10.

The LOEL used to calculate C' was 200 µg Hg/day/70 kg (2.86 µg/day/kg) individual. This LOEL was apportioned to each body of water according to the average individual intake of total mercury from the body of water. The average individual daily intake was calculated from the amount of each fish species consumed per day and the average concentration of total mercury in edible tissue for that species (see Table 18 for details). Apportioning the total daily intake of 200 µg Hg/day/70 kg according to average individual intake from each body of natural water, the LOEL for freshwater was calculated as 22.5, for estuarine and coastal as 19.5, and for open oceans as 158 µg/day/70 kg individual.

The average practical bioconcentration factor (PBCF) was chosen as the median value for each species in each body of water. The median PBCF for freshwater is 5,500, for estuarine and coastal water is 3,760, and for open ocean it is 9,000. Given the large values of PBCF, the contribution of drinking water to total daily intake is negligible so that assumptions concerning the chemical form of mercury in drinking water become less important.

Substituting in equation (4) the apportioned values of LOEL, d, and PBCF for each body of water, and using a safety factor of 10 the following criteria were calculated: freshwater 196 ng/l; estuarine-coastal waters, 108 ng/l; and open ocean 143 ng/l (Table 19). The safety factor of 10 is intended to take into account individual differences in habits of fish consumption and in susceptibility to the toxic effects of methylmercury, including prenatal exposures.

In view of the assumptions and approximations involved in the derivation, the values for the criteria will be rounded to 2 significant figures. Thus three levels are as follows: freshwater, 0.19 µg/l; estuarine-coastal, 0.11 µg/l; and open oceans, 0.14 µg/l.

Since Hg is extensively bioaccumulated in the tissures of open ocean organisms and these marine species constitute the major portion (i.e., approximately 65 percent) of total ingested fish (Table 19), the criterion calculation of primary significance to human health is one that incorporates the ingestion of open ocean fish or shellfish as well as freshwater and estuarine/coastal aquatic organisms. This criterion level reflects the intake of 2 liters of water per day and the daily intake of 0.00172 kg of freshwater aquatic organisms, 0.00478 kg of estuarine/coastal organisms, as well as 0.0122 kg of open ocean organisms (Table 19). It is calculated as:

$$C" = \frac{\text{(LOEL)/uncertainty factor}}{2 + (0.00172 \times PBCF_f) + (0.00478 \times PBCF_{ec}) + (0.0122 \times PCBF_o)} \quad ...5$$

where:

LOEL = 200 μg/day

Uncertainty factor = 10

$PBCF_f$ = Practical BCF (5500) for Hg in freshwater organisms

$PBCF_{ec}$ = Practical BCF (3760) for Hg in estuarine/coastal organisms

$PBCF_o$ = Practical BCF (9000) for Hg in open ocean (marine) organisms

2 = daily water consumption in liters

Substituting for equation (5),

$$C" = \frac{200\ \mu g/day/10}{2 + (0.00172 \times 5500) + (0.00478 \times 2760) + (0.0122 \times 9000)}$$

$$= \frac{20\ \mu g/day}{139.2}$$

$$= 0.144\ \mu g/l \text{ or } 144\ ng/l$$

This concentration would be protective against the adverse effects of Hg via daily ingestion of 2 liters of water and consumption of contaminated aquataic organisms from all sources (freshwater, coastal/estrarine, and open ocean).

The inclusion of open ocean marine organisms in this calculation represents an effort to consider all pertinent sources of human exposure to Hg. However, the use of ingestion and bioconcentration data for marine species in this criterion derivation is an additional important factor not used in other documents of this series. Contributions from non-fish food sources are not considered since levels of mercury in these materials are so low as to be undetectable using available analytical techniques (NAS, 1978).

In summary, based on the use of human epidemiological data and an uncertainty factor of 10, the criterion level of mercury corresponding to an acceptable daily intake of 2,86 μg/kg, is 144 ng/l. Drinking water contributes approximately 1 percent of the assumed exposure while eating contaminated fish products accounts for 99 percent. The criterion level can similarly be expressed as 146 ng/l if exposure is assumed to be from the consumption of fish and shellfish products alone.

Comment on Criteria

Experimental investigation indicated that when fish are exposed to methylmercury, a rapid uptake phase is completed in about 2 to 3 months (Ottawa River Project, 1976). Thereafter, uptake may continue but at a slower pace. Thus, it seems reasonable to regard the criteria as a time-weighted average concentration covering a period of 2 months or so. In other words, it should not be regarded as an instantaneous value that should never be exceeded even for brief periods of time.

In this document a total of four criteria have been calculated using various assumptions relative to average daily intakes of aquatic organisms from fresh, estuarine/coastal, and open ocean waters. The criteria have been calculated by an arithmetical procedure using the best available evidence for the important parameters, e.g., LOEL, BCF and average daily intake of fish. It should be noted, however, that of the four values derived, the recommended criterion of 0.14 μg/l is based on a total daily consumption of 18.7 g of freshwater, estuarine, and marine organsims and an intake of 2 liters of water daily.

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